UNIVERSITÄT
BERN

Master Biomedical Engineering

Annual Report 2012

Master of Science in Biomedical Engineering

Contents

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Introduction

2012 in Retrospect

The mission statement of this master's program is ambitious: "Train multidisciplinary engineers to deliver scientifically founded and cost-effective solutions for biomedical problems in research and industry". This statement reflects the aim for a flexible educational platform in a quickly evolving economical and social environment that is anchored on strong scientific foundations, but privileges a problem solving approach that is aware of the rules of the medtech market and the strong constraints of contemporary health care systems. It is therefore an honor but also a challenge to take over the responsibility for this master's program in Biomedical Engineering from Prof. Lutz Nolte, who initiated it from scratch six years ago. This is a rather short history for a successful program that welcomed 47 new students, delivered 45 master's degrees and organized a highly successful Biomedical Engineering Day in 2012.

One keyword for the past year was consolidation: consolidation of the cooperation with the Bern University of Applied Sciences and consolidation of the administrative processes within the study coordination. New faculty members of the Bern University of Applied Sciences joined the program and their contribution is highly appreciated. Prof. Stefan Weber was appointed as a full professor for Image-Guided Therapy and as the new chair of the ARTORG Center within the Faculty of Medicine of the University of Bern. Besides these appointments, he accepted to share his expertise in higher education by heading the specialization module in Image-Guided Therapy of the master's program. The regulations of the master thesis were updated in an attempt to simplify the management of intellectual property, clarify the role of examiners and supervisors and request an executive summary from every student. The recruitment of new students was refined by requesting a motivation letter and by abandoning automatic admissions.

A second keyword of 2012 is acknowledgement: acknowledgement to the numerous lecturers and acknowledgement to the study coordination. More than 80 lecturers contribute to the master's program covering Biomedical Sciences as well as numerous topics in Biomedical Engineering and share a broad spectrum of academic, medical and industrial experience. This diversity is undeniably one of the strengths of this program and represents a rather unique feature in the Swiss academic landscape. I am very grateful for their ongoing support, and especially to those providing medical education in addition to heavy teaching loads for the curricula in Human Medicine. In 2012, three new courses, namely Biomaterials, BioMicrofluidics and Medical Image Analysis Lab, were introduced. They were highly successful and I would also like to express my special thanks to the initiating teachers. Besides the teachers, the study coordination did the essential part of the work in this Master Program and I am very grateful for the motivation and diligence of the whole team including Ulla Jakob-Burger, Volker Koch, Alexandra Neuenschwander Salazar, Mauricio Reyes and Julia Spyra.

In this third annual report, we are glad to share not only the organization, statistics and life of the master's program, but also an extensive overview of the diverse research topics in Biomedical Engineering that were investigated in the master theses. The authors of these theses represent the core added value of this program and I wish them favorable winds for their professional careers.

Philippe Zysset
Program Director

Organization

Master of Science in Biomedical Engineering

Ph. Zysset
Program Director

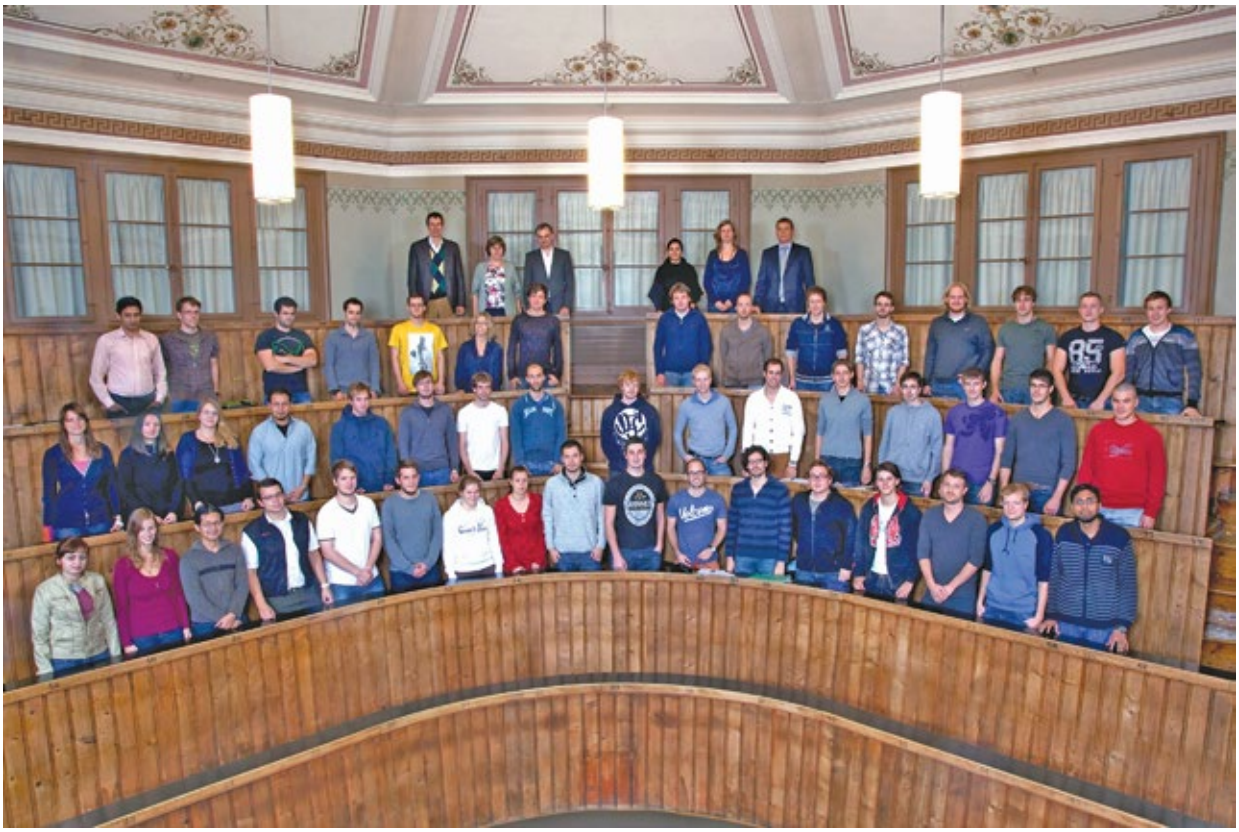
U. Jakob-Burger
Study Coordinator

M. Reyes
Master Thesis Coordinator

V. M. Koch
Deputy Director

A. Neuenschwander Salazar
Study Coordinator

J. Spyra
Study Coordinator



BME First Year Students 2012, Alter Hörsaal der Anatomie, University of Bern.

Structure of Courses in the Master's Program

Since the start of the Master's Program Biomedical Engineering in March 2006, the constant effort to improve the quality of our curriculum has resulted in substantial changes of the course structure over the past years. The first curriculum consisted of a number of individual courses which were either mandatory or elective, but their coherence with regards to contents was in most cases not expressed by a defined structure. However, two major modules (formerly called "focus areas") already existed.

As of Fall Semester 2009, all courses were grouped in a strictly modular way in order to enhance both the clarity and the complexity of the curricular structure. A main idea was to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called "Image-Guided Therapy".

The Curriculum

Duration of Studies and Part-Time Professional Occupation
The full-time study program takes 4 semesters, which corresponds to 120 ECTS points, one ECTS point being defined as 25-30 hours of student workload. It can be extended to a maximum of 6 semesters. When a student decides to complete the studies in parallel to a part-time professional occupation, further extension is possible on request. To support regular part-time work, mandatory courses take place (with rare exceptions) on only 3 days per week.

Basic Modules
The basic modules provide the students with the necessary background to be able to fully understand the highly complex subject matter in the specialized courses. All students with an engineering background (for all other students, individual study plans are set up which may contain certain variations) have to complete all courses in the Basic Modules Human Medicine, Applied Mathematics, Biomedical Engineering, and Engineering Mechanics. In the first semester, all courses belong to this group, whereas in the second and third semester, the courses from the basic modules make up for 25-30%.

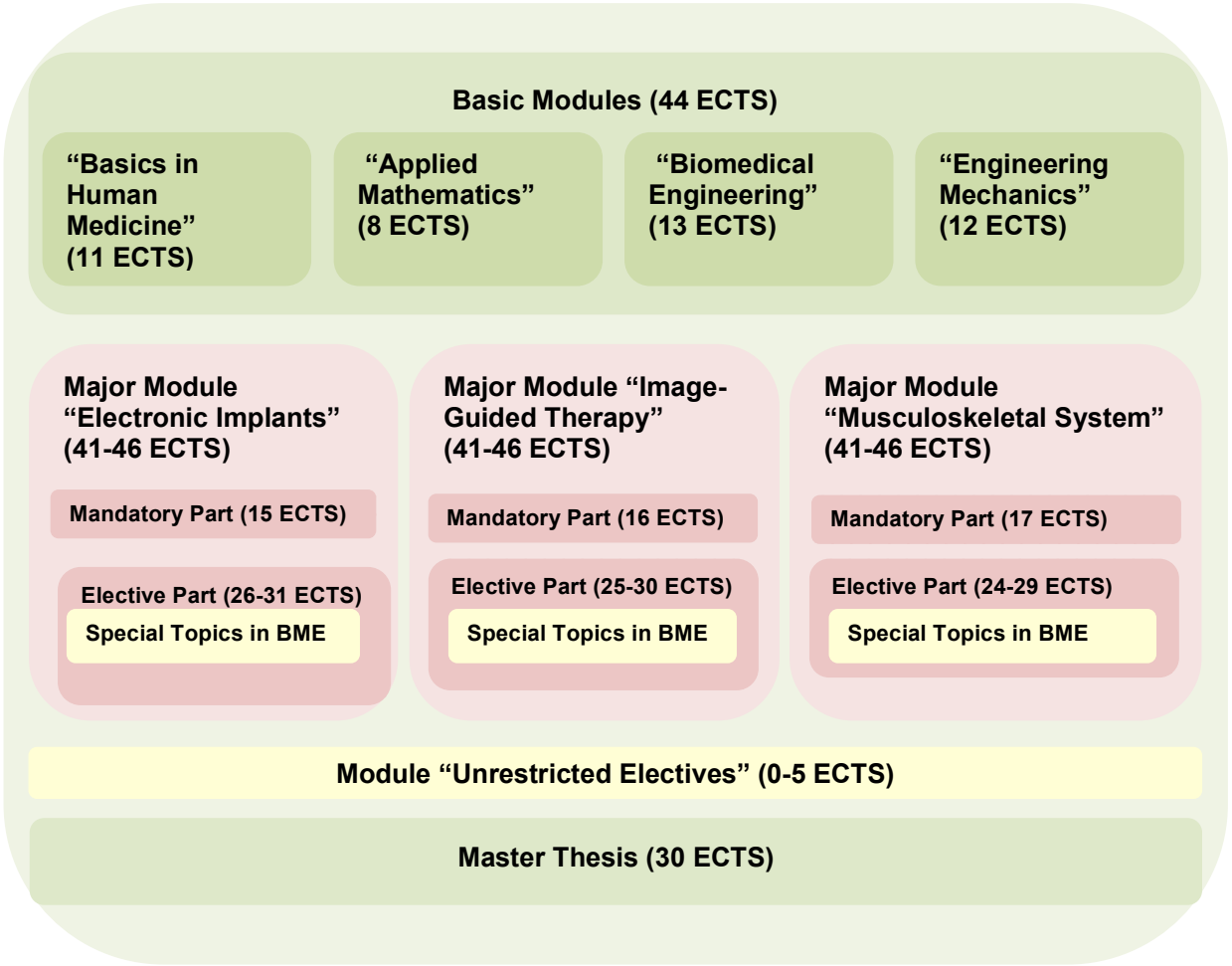
Major Modules
The choice of one of three major modules Musculoskeletal System, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization. Approximately one third of the major modules consists of mandatory courses. In the elective part of the major module, the student is allowed to select any course from the list of courses in the master's program, giving rise to a high degree of diversity and flexibility and allowing for numerous course combinations. However, this freedom makes it somewhat difficult for the student to make reasonable choices regarding professional prospects.

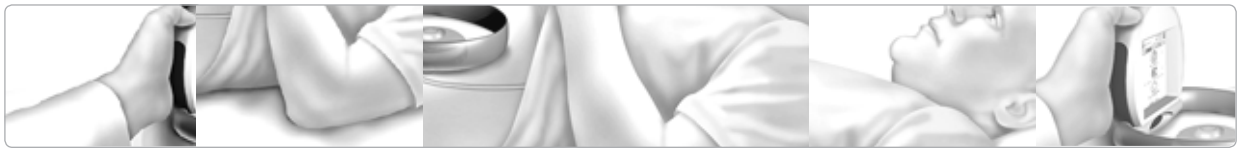
This is why the responsible lecturers developed a recommended study plan to guide the students through the course selection process and to avoid organizational problems such as overlapping courses. If a student follows the recommended path, he or she can be sure to establish a sound professional profile.

Module "Special Topics in Biomedical Engineering"
In order to meet an increasing demand for continuing education in the medical technology industry, the Special Topics in Biomedical Engineering have been developed. Scientists from institutions affiliated to the Medical Faculty of the University of Bern - the Artificial Organ (ARTORG) Center for Biomedical Engineering Research as well as the Institute of Surgical Technology & Biomechanics (ISTB) – established the course curricula in close collaboration with representatives from the leading medical technology companies in Switzerland. Courses have been designed to convey state-of-the-art knowledge in many future-oriented areas at the interface between applied scientific research and industrial research and development on a high level. Apart from contributing a hands-on aspect to the studies, thus complementing the theoretical foundation which is laid in the basic modules, these courses provide an excellent opportunity for industry professionals to deepen and enlarge their knowledge in selected areas of Biomedical Engineering. In 2012, the course list was augmented by the courses Biomaterials, BioMicrofluidics, and Medical Image Analysis Lab. Formally, this module has been integrated into the elective parts of the major modules.

Module "Unrestricted Electives"
Unrestricted electives can be chosen freely by the student from the entire curriculum of the University of Bern and the Bern University of Applied Sciences, Department of Engineering and Information Technology. Of these courses, a maximum of 5 ECTS points is credited. It is advisable to select courses which fit into the context of the student's study plan, either to make up for missing knowledge or to add new and interesting aspects to the individual study program.

Master's Thesis
The last semester is dedicated to a master's thesis project on an individually suited topic in an academic research group or, for particular cases, in an industrial research and development environment. As a rule, all 90 ECTS points from the course program have to be completed, thus ensuring that the student is able to fully concentrate on the challenges imposed by exciting research activities. The master's thesis includes the thesis paper, a thesis presentation and defense as well as a one-page abstract for publication in the Annual Report of the master's program.





Major Modules

Electronic Implants

V. M. Koch

Electronic implants are devices like cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications become feasible and this exciting area is growing rapidly. For example, cochlear implants provide already approximately 200'000 people a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words.

There are many more applications for electronic implants beyond treating heart problems, hearing loss or blindness. For example, there are electronic implants that treat obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

In this module, students will learn about the basics of electronic implants. This includes: sensor and measurement technology, signal processing and analysis, microcontroller programming, actuator technology, and miniaturization of micro-electro-mechanical systems. Application-oriented topics are also taught, e.g., cardiovascular technology and biomedical acoustics.

Since the development and manufacturing of electronic implants is highly complex and since it involves many different disciplines, it is not the goal of this major that students are able to develop an electronic implant on their own but rather to be able to work successfully in a project team that develops electronic implants.

Students may already apply their knowledge as a part-time assistant in a laboratory and/or during their master's projects. After finishing the degree program, a wide variety of career paths are available, ranging from research and development to project and product management. Many well-known companies in Switzerland work in this field, e.g., Codman and Phonak Acoustic Implants. This list is, of course, not complete. For example, many „traditional" implants manufacturers have recently become interested in electronic implants, e.g., to measure forces in knee implants.

Example of an electronic implant:
The Programmable Infusion System is the new programmable infusion system from CODMAN® (a Johnson & Johnson company), indicated for the intrathecal delivery of Baclofen for the treatment of severe spasticity and preservative free morphine sulfate for chronic pain (benign or malignant).

Image-Guided Therapy


Ph. Cattin, S. Weber

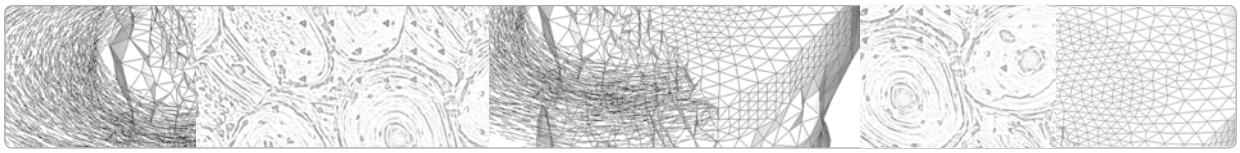
Image-Guided Therapy refers to the concept of guiding medical procedures and interventions through perceiving and viewing of medical image data, possibly extended by using stereotactic tracking systems. Medical imaging typically relates to a great variety of modalities ranging from 2D fluoroscopy and ultrasound to 3D computed tomography and magnet resonance imaging, possibly extended to complex 4D time series and enhanced with functional information (PET, SPECT). Guidance is realized by various means of determination of spatial instrument-to-patient relationship and by suitable visualizations. Image guidance is very often accompanied by other surgical technologies such as surgical robotics, sensor enhanced instrument systems as well as information and communication technology.

Prediction error in scale (green dots) of a liver for tumour ablation (Ph. Cattin).

Students of the IGT module will be introduced to the fundamentals of the above mentioned clinical and technical aspects of image-guided therapy. They will receive an overview of currently applied clinical standards as well as an overview of latest advancements in research. Successful students will be able to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches to IGT. This will enable further careers both in the industrial and academic sector.

Mandatory courses of this module are concerned with the fundamentals of Signal and Image Processing and Medical Image Analysis. Furthermore, fundamental aspects of stereotactic image guidance, tracking, patient-to-image registration and basic clinical applications are taught in the course Computer-Assisted Surgery. Recent trends and fundamental aspects in surgical robot technology, minimally-invasive procedures and its applications within IGT are introduced in the course Medical Robotics. Additional elective courses extend students competencies in related areas such as computer graphics, pattern recognition, machine learning, and regulatory affairs.

Modern image guidance based on computer tomography and sonography for support during complex surgical procedures on the liver helps to improve outcomes (S. Weber).



Major Modules

Musculoskeletal System

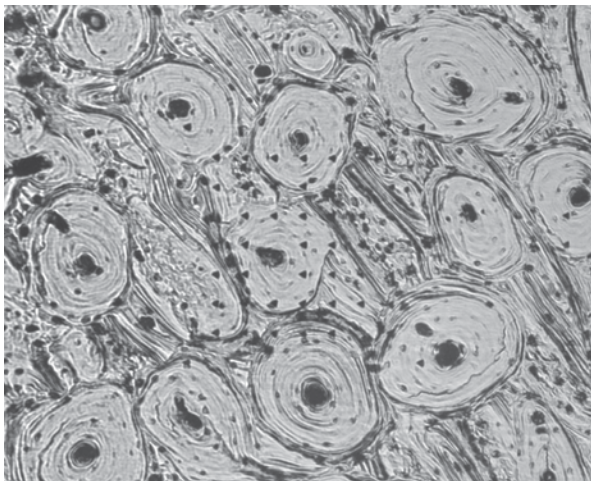
Ph. Zysset

The musculoskeletal system is the structural basis for our physical activities and its health has a profound influence on our quality of life. Musculoskeletal injuries and pathologies are the most costly ailments facing our health care systems, both in terms of direct medical costs and compensation payments related to loss-of-work. In this module, students will gain a comprehensive understanding of the multi-scale organisation of the musculoskeletal system, combining knowledge from the cell, tissue, organ to the body level. They will learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechanobiology. Students will learn to draw connections between musculoskeletal tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of orthopaedics, dentistry, rehabilitation and sports sciences.

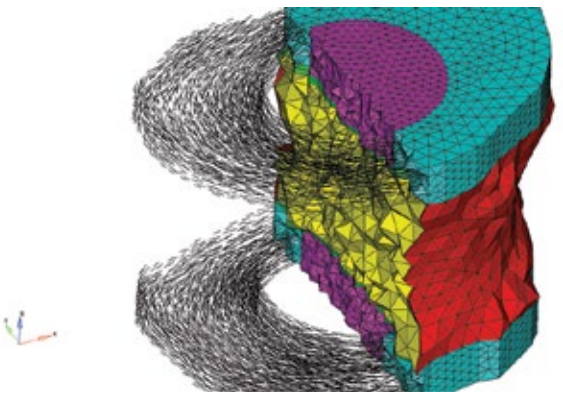
The mandatory courses in this module provide the student with fundamental knowledge of functional anatomy, tissue engineering, tissue biomechanics and finite element analysis. This provides an overview of the functional adaptation of the musculoskeletal system to the demands of daily living, and the necessary conditions for its repair and regeneration. This major module requires a prior knowledge of mechanics, numerical methods and related engineering sciences, as many of the mandatory and elective courses build upon these foundations. Elective courses allow the students to extend their competence in a chosen direction, gaining knowledge in analytical methodologies, medical device design, orthopaedics, or rehabilitation.

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application and the lab bench top to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of past thesis projects include the investigation of a collagen derived matrix (CDM) for treatment of articular cartilage lesions, the visualization of microcracks in cortical bone, the evaluation of a motion tracking system for gait rehabilitation robotics or the development of an enzyme-driven intervertebral disc degeneration model.

Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering or development of biomaterials. Most of the major companies in the fields of orthopaedics, rehabilitation engineering and pharmaceuticals are strongly represented within the Swiss Medical Technology industry and continue to experience growth, therefore driving a demand for graduates of this major module. At the interface between biomedical engineering and clinical applications, graduates may also pursue careers related to the evaluation and validation of contemporary health technology, a cornerstone for future policies on the adoption of these new methods in the highly competitive health care domain.



Nanoindentation in Haversian bone (J. Schwiedrzik).



Finite element model of a human vertebral segment (G. Maquer).

List of Courses

Applied Biomaterials
Biological Principles of Human Medicine
Biomaterials
Biomedical Acoustics
Biomedical Instrumentation
Biomedical Laser Applications
Biomedical Signal Processing and Analysis
BioMicrofluidics
Cardiovascular Medicine and Engineering
Computer Assisted Surgery
Computer Graphics
Computer Vision
Design of Biomechanical Systems
Electrical Engineering
Engineering Design
Engineering Mechanics I
Engineering Mechanics II
Finite Element Analysis I
Finite Element Analysis II
Functional Anatomy and Histology
Functional Anatomy of the Locomotor Apparatus
Health Technology Assessment
Intelligent Implants and Surgical Instruments
Introduction to Medical Statistics
Introduction to Signal and Image Processing
Machine Learning
Management
Materials and Technologies in Dentistry
Medical Image Analysis
Medical Image Analysis Lab
Medical Robotics
Microelectronics
Microsystems Engineering
Molecular Biology
Numerical Methods
Osteology
Physiology
Practical Course in Tissue Engineering
Principles of Medical Imaging
Programming of Microcontrollers
Regulatory Affairs and Patents
Rehabilitation Technology
Reliability of MEMS for Medical Applications
Technology and Diabetes Management
Tissue Biomechanics
Tissue Engineering

Practical Course in Tissue Engineering: Ben Gantenbein with some of his students in the lab at the ISTB.

New Courses

Biomaterials



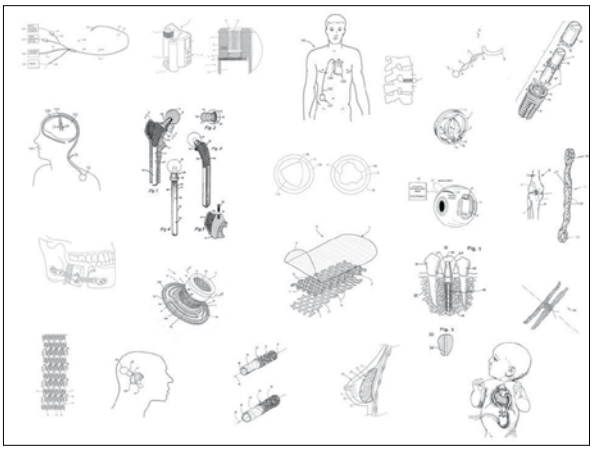

M. Bohner, L. Eschbach, R. Heuberger, R. Luginbühl (without picture), J. Sague

The course "Biomaterials" is well established and has been an integral part of the curriculum of the Master of Science in Biomedical Engineering for many years. Due to administrative changes the course was restructured and given the first time in fall 2012 by senior scientists of the RMS Foundation. Based on the application driven material research carried out at the RMS Foundation, the course teaches the fundamentals in biomaterial sciences in an object lesson approach. "Biomaterials" is a very broadly defined field in science, but ultimately, it is all about a material which is brought into contact with a human being.

The course starts with general material chemistry, recapitulating the atomic structure and the relationships between the arrangements of atoms, ions, or molecules comprised in materials, and it classifies them based on their structural properties. Understanding the solid state of materials and their structural diversity is considered key for successful engineering, designing and processing of medical devices. Special lessons on metals, ceramics, polymers and natural materials elucidate the basic properties of the respective materials and are all exemplified in object lessons. In order to assess the solid state materials, proper selection of analytical techniques and the interpretation of the results is also a prerequisite. While the proper selection of the solid state material is utmost important for the mechanical properties of a given device, surfaces define to a large degree the interaction with the biological surrounding of medical device. Thus, aspects of coating technologies, surface finish or chemical derivatization of the surfaces and the influence on protein and cells are also taught in special chapters. The term "biocompatibility" is approached in a general term showing the students the legal requirements of testing, how to rate some of the biological assays, and what to expect from biocompatibility testing.

Last but not least, specified medical devices are assigned to the students as homework which look into the topic in small groups and present their finding on the device, i.e. on its special characteristics, on the choice of materials, and on the success and risks of failure.

After the course, the students should be able to evaluate in a lateral thinking approach the performance of a medical device based on material selection and combining all the aspects of material properties, surface engineering, material processing and device design.



The diversity of medical implants.

BioMicrofluidics

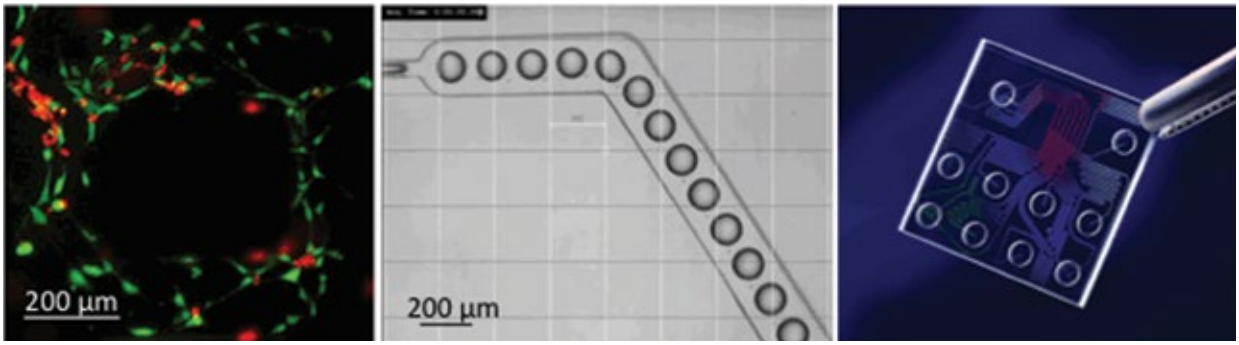

O. Guenat, E. Marconi

Bio-microfluidics, also often called "lab-on-chip" or "cells-on-chip", has become a major research field in the last ten years. It deals with the accurate control and the automated manipulation of tiny volumes of fluids (microflui-dics) for the investigation of biological compounds, such as DNA, proteins or cells. The Bio-microfluidics market is estimated to be worth 1 billion US$, with a steady 20% annual growth in areas like drug discovery, diagnostics, toxicology and personalized medicine.

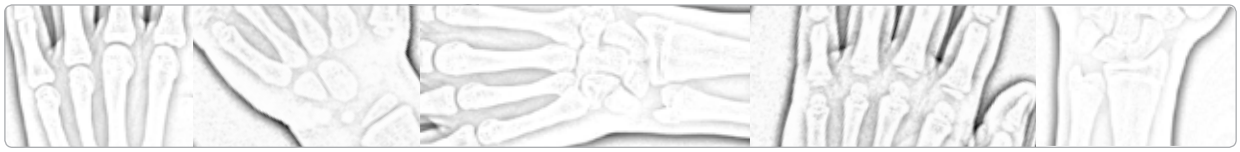
In this course, the development of bio-microfluidic devices will be looked at from three different perspectives. First, students will learn why minute amount of solutions confined in micro- and nanochannels can interact much more rapidly and efficiently than in macrosystems. At the micro- and nanoscale, the impact of phenomenon, such as surface tension, electrokinetic effects, molecular diffusion, heat transfer are much more important than at the macroscale level. Second, the technologies used to fabricate such microsystems will be considered. To structure tiny microwells in which cells are cultured, or nanochannels in which DNA strains are unfold, techniques that originate from the microelectronic industry are used, as well as other technologies, such as PDMS rapid prototyping, hot embossing and injection molding, enabling the mass production of cheap and disposable chips. Finally, the third part of the course will deal with the analysis and the description of several applications and examples. Several lectures will focus on advanced microfluidic systems, in which cells can be trapped, cultured and analyzed. Such systems have dimensions that are very similar to mammalian cells and thus are ideal to investigate biological effects. Furthermore, these tools have the potential to replace standard cell culture systems (Petri dish), since they make it possible to reproduce the in-vivo conditions, such as the shear stress induced by the blood stream, the three-dimensional architecture of the tissues and the extracellular matrix. In the near future, organs-on-chip (liver-on-chip, blood-on-chip, lung-on-chip, etc.) will appear on the market and will replace or at least reduce animal testing, that are very expensive and often not very predictive for humans.

Successful commercial examples of microfluidic products aimed for biological applications will also be presented and analyzed during the course, such as the chips for DNA and protein analysis of Affymetrix and Caliper Life Sciences (Perkin Elmer). Other cutting-edge products from emerging start-ups will also be presented, such as those from CellAsic, Bellbrookelabs, InSphero, Fluidigm, to name a few.

At the end of the course, the students will understand the fundamental phenomena that are used in microfluidics and will know how to design and fabricate simple bio-microfluidic systems, based on physical, technological, material, biological and economic constraints.



Left: live/dead assay of fibroblasts cultured in a circular microchannel. Middle: 100 µm diameter alginate beads created by flow focusing. Right: DNA electrophoretic chip from the company Caliper Technologies (Perkin Elmer).



New Courses

Medical Image Analysis Lab


Ph. Cattin, M. Reyes

The *Medical Image Analysis Lab* lecture was held for the first time this year. The main aim of this course was to introduce the students to a real yet unsolved clinical problem. In groups of mostly three students their task was to tackle the given clinical problem using methods and techniques they learned throughout the course. In the weekly meetings, the students were continuously supported by the lecturer that pointed students to alternative solutions and/or helped them to assess possible solutions and ideas. In the last week of the semester, a competition was held, where additional new data sets had to be automatically processed by the groups own software. These results were then compared to the gold standard solution performed by an experienced radiologist.

The clinical task given to the class was the assessment of the joints in planar X-rays of children's hands, see figure. These types of images are regularly captured in pedeatry to estimate the maturity, i.e. bone age, of a child's skeletal system. Bone age can significantly differ from a child's real age and is clinically used to diagnose and predict for example what the final height will be, when a child will enter puberty and to estimate the age of a child if not known for certain reasons. Besides the diagnostic purposes the bone age is also used to track the progress of treatments that affect growth such as hormonic dysregulation or genetric growth disorders but they are also used in orthopedic or orthodontic problems in which the timing and type of treatment must be carefully guided by the child's predicted growth.

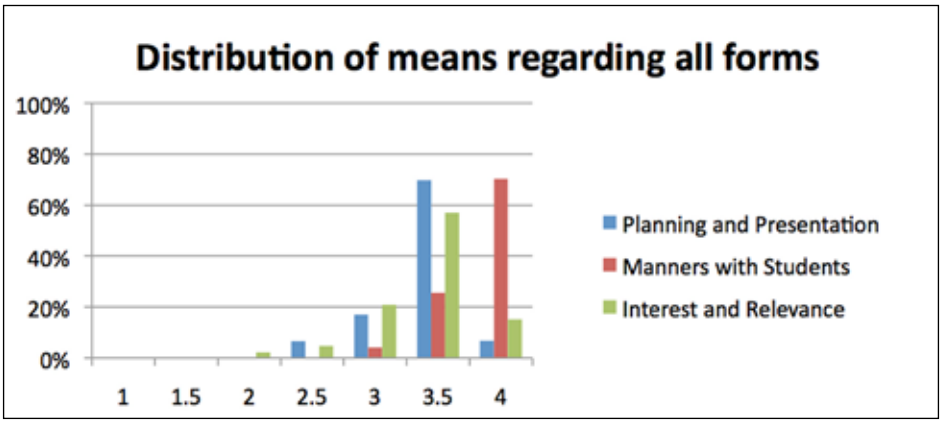
The range of complexity and the sophistication of the methods the different groups applied for the various tasks varied significantly. To the surprise of all students a clever idea combined to simplify the problem was often on par with a mathematically well founded complex approach.
In this more practical lecture the students not only learned to work in groups and how to split up the work but they also had to produce results on a given deadline.

Handplate of a 4 year old female.

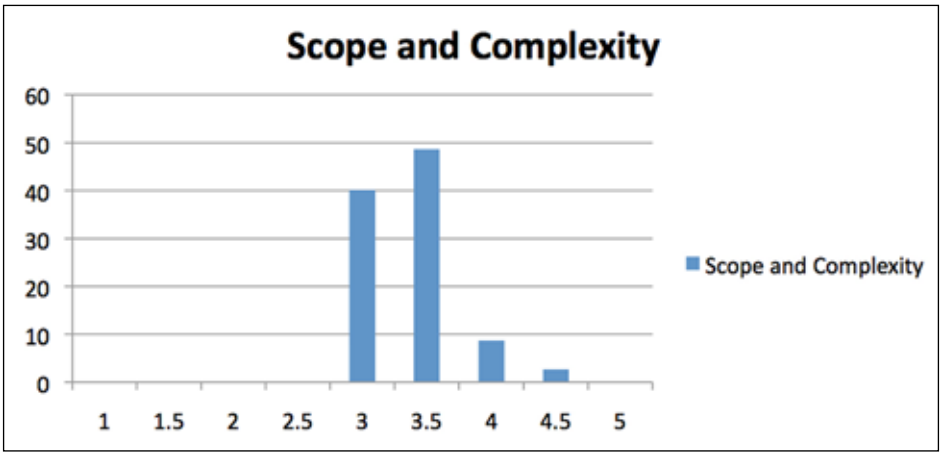
Handplate of a 16 year old male.

Evaluation of Courses in 2012

Like in the previous year, a centralized evaluation was performed in the master's program in 2012 according to the guidelines of the University of Bern. Both spring and fall semester were considered leading to 47 course evaluations involving more than 800 forms in total. The results regarding all forms (see below) reveal that the students are very satisfied with the course program and that the courses are interesting and demanding at the same time.



1: very poor 2: poor 3: good 4: excellent



1: far too narrow/narrow 3: just right 5: far too high/wide

Faculty

Acikgöz Ersoy Dr., Bernur
Albrecht Prof. Dr., Christiane
Altmann, Martin
Andres Prof. Dr., Anne-Catherine
Baum PD Dr., Oliver
Bohner Dr., Marc
Büchler PD Dr., Philippe
Burger PD Dr., Jürgen
Busato Prof. Dr., André
Cattin Prof. Dr., Philippe
Caversaccio Prof. Dr., Marco-Domenico
Czerwinska Prof. Dr.-Ing., Justyna
Debrunner Prof., Daniel
de Haller Dr., Emmanuel
Diem Prof. Dr., Peter
Dommann Prof. Dr., Alex
Egger Prof. Dr., Marcel
Eglin Dr., David
Eschbach Dr., Lukas
Favaro Prof. Dr., Paolo
Firouzi Prof. Dr., Elham
Frenz Prof. Dr., Martin
Gantenbein Prof. Dr., Benjamin
Geiser Kamber Prof. Dr., Marianne
Götte Prof. Dr., Josef
Greenburg Dr., Alain
Guenat Prof. Dr., Olivier
Hänssgen, Kati
Haschtmann Dr., Daniel
Heuberger Dr., Roman
Hlushchuk Dr., Ruslan
Hoenes Dr., Hoachim
Hofer Dr., Ulrich
Hofstetter Prof. Dr., Wilhelm
Hoppeler Prof. Dr., Hans-Heinrich
Hunt Prof. Dr., Kenneth
Hüsler Prof. Dr., Jürg
Ilgenstein Dr., Bernd
Jacomet Prof. Dr., Marcel
Jäger Prof. Dr., Kurt
Jensen Prof. Dr., Björn
Jungo Dr., Markus
Justiz Prof. Dr., Jörn
Keppner Prof. Dr., Herbert
Koch Prof. Dr., Volker
Kompis Prof. Dr., Martin
Kowal Prof. Dr., Jens
Kucera Prof. Dr., Jan
Lechmann, Beat
Lerf Dr., Reto
Luginbühl Dr., Reto
Lurman Dr., Glenn
Mack Dr., Alexander
Marconi Dr., Emanuele
Moser Dr., Walter
Mougiakakou Prof. Dr., Stavroula
Müller Prof. Dr., Bert
Mussard Prof., Yves
Neels Dr., Antonia
Nef Prof. Dr., Tobias
Nesic PD Dr., Dobrila
Nevian Prof. Dr., Thomas
Niggli Prof. Dr., Ernst
Nolte Prof. Dr., Lutz-Peter
Peterhans Dr., Matthias
Reyes PD Dr., Mauricio
Sague Dr., Jorge
Schäfer PD Dr., Birgit
Schenk, Samuel
Schittny Prof. Dr., Johannes
Senn Dr., Pascal
Senn Prof. Dr., Walter Martin
Stahel Prof. Dr., Andreas
Sterchi Prof. Dr., Erwin
Stoyanov Dr., Jivko
Streit Prof. Dr., Jürg
Tschanz Dr., Stefan
Ullrich Dr., Nina
Vogel Prof. Dr., Rolf
Weber Prof. Dr.-Ing., Stefan
Wolfram Dr., Uwe
Zheng PD Dr., Guoyan
Zimmermann Prof. Dr., Heinz
Zwicker Prof. Dr., Matthias
Zysset Prof. Dr., Philippe

BME Lecturers in Le Locle

Although the sun was timidly shining on the 9th of February 2012, the day was freezing cold. We went from Bern Wankdorf train station towards Neuchatel to pick up the other lecturers and headed to Le Locle for the annual lecturers' event, organized for the third time. Snow covered Le Locle, although at an altitude of nearly 1000m, surprised us with a pleasant temperature of -1°C; it felt almost like spring!

We were welcomed in a cosy room by Juergen Burger, who introduced the complex Johnson and Johnson company group, showing us many different products, interests and technologies this company has developed and acquired over the years – from a traditional baby shampoo to neurological implants.

J&J is the 4th world largest employer in the US, consisting of over 250 companies in 60 countries. And it all started with a Bandaid! The list of companies that were ultimately acquired under the J&J and DePuy umbrella is rather long. One interesting detail was the collaboration between Medos and Tissot which resulted in the development of a hydrocephalus shunt. This brought about the reason for the presence of J&J in Switzerland – quite simply: a famous high precision microtechnology environment, well-known universities, vicinity of subcontractors, an easy communication with authorities, and finally cantonal support.

BME lecturers and staff enjoy wine and cheese fondue.

After being swapped by the diversity of J&J activities, Yves Girardin presented the MedStream Pump from Codman. MedStream is the first programmable infusion pump for the treatment of chronic pain and muscle spasticity. The pump is in direct contact with cerebral fluid, placed in the peritoneum, has a lifetime of 8 years, and does not require frequent battery exchanges due to low energy requirements. The control unit is implanted under the skin in a 20 minutes operation. The engineering started in 2003 and it was approved in 2008 in the EU, and in 2010 in the USA. With 500 patients already operated, the target is 15'000 yearly.

The next presentation was about Certas, a programmable valve for the patients suffering from hydrocephalus, known as water in brain as a consequence a buildup of cerebrospinal fluid inside the skull that leads to brain swelling. The patients suffer from an increased intracranial pressure inside the skull and progressive enlargement of the head, convulsion, tunnel vision, and mental disability. Hydrocephalus can also cause death. The second generation of Certas valve, approved in 2011 in the EU and in the US, is easy to program, with 8 different pressure settings, an indicator tool, and an optional attachable Bactiseal catheter containing antibiotics.

After a small refreshment break, we made two tours – the MedStream production tour and the titan workshop from Spine tour. The surprise was – labelling in French – unexpected at an American company, although in the heart of French-speaking Jura. We learnt that it takes 6 weeks to produce the MedStream pump. Starting with quality inspection of pieces coming from various suppliers, proceeding to subassembly (26 laser welding in 26 fixations including microscopic inspection of every step!), to mechanical testing, first round of packaging, sterilization, and final packaging. All electronics parts are done in a special dust-free clean lab, where you need to get electro-static discharge before you are allowed to enter. The pumps are produced in batches, depending on a phase in the production line, the number per batch ranges between 7 to 75 pieces.

Depuy Spine is the second largest spine company in the world, developing innovative orthopaedic and neurosurgical products that address key areas of spinal care, including cervical, aging spine, vertebral body replacement,

Faculty

minimally invasive surgery, and the emerging area of biologics. We observed the production line of beautifully colourful screws, each colour corresponding to the particular diameter and length. We were impressed yet again with various quality control points and instruments developed to ensure high quality. Each screw comes with a specification sheet and ready to use for the orthopaedic surgeon. We saw a newly acquired station for packaging and control, which allows time gain of several days, custom produced by a company Komax System AG from La Chaux-de-Fonds.

The evening was already on its way, the J&J building in the dark surrounded by the fields of snow. With so much interesting novel information to process, our brain cells were in a prompt need for nourishment. Soon, we were driving to a small restaurant somewhere up in the woods above the lake of Neuchatel for a fondue. Few schnapps allowed for a lively atmosphere of scientific discussions as well as threats of loosing bread in the fondue and being punished according to Asterix and Obelix among Helvetii. With the lake being not so far and the temperature deeply below zero, the threat appeared rather scary! The drive back seemed quick, as we discussed possibilities on how to motivate more lecturers to join this nice event next year.

Dobrila Nesic, DKF University of Bern

Company Visit

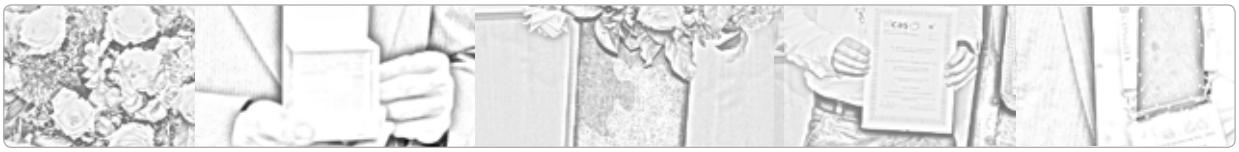
BME Students visit Straumann
This year's excursion of about 20 students of the Biomedical Engineering Master's Program went to the dental implant prodcution plant of Straumann in Villeret. Straumann is a leading producer of dental implant technologies and the excursion offered a unique insight into modern production technologies and capabilities.

After arriving in Villeret a quick introduction to the history and the market postion of the company was given by the head of production. In particular, it was interesting to hear that the company actually started of as metallurgy venture producing alloys for the swiss watch industry and just started to enter the field of medical devices in the 70ies.

After this introduction, the students got a tour through the production facility itself including the clean area. This was especially nice, since it led through the whole process of implant procuction from the raw material to the final shipping. The group of students was devided into two so that we had good opportunities to ask questions and discuss certain steps.

A certain highlight of the outing was the informative lunch after the tour through the plant. Two researchers from the R&D department of Straumann in Basel were able to join the lunch. This provided the opportunity to get into deeper discussions about the company, the products, and the job as a R&D engineer. All in all this informative lunch rounded up a wonderful trip to an interesting company!

Uwe Wolfram, ISTB University of Bern



Biomedical Engineering Day 2012

The industry, medical doctors, and engineers meet for the Biomedical Engineering Day at the Inselspital in Bern with great success

On May 25, 2012, the Biomedical Engineering Day took place in the auditorium Ettore Rossi at the Inselspital in Bern. The Master in Biomedical Engineering program of the University of Bern organized this event for the fourth time.

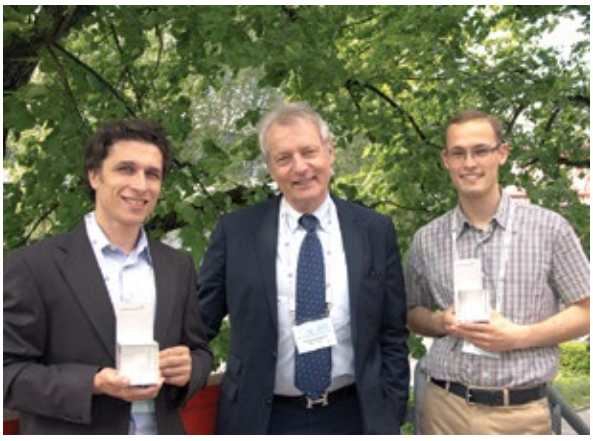
The event is an efficient platform in Switzerland for networking of Master and PhD graduates and Swiss and international medical technology companies. This year's companies introduced themselves through oral presentations and gave insight into their commercial activities and their company philosophies as well as showed their demands on junior employees. Students thus had the opportunity to get to know potential future employers and contact them directly. This was made possible between the sessions in personal conversations and at the exhibitors' booths.

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Institute for Surgical Technologies and Biomechanics as well as the Bern University of Applied Sciences, a partner within the master's program, used the possibility of presenting current research projects to more than 320 participants. Interestingly, Master and PhD students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too.

Besides company representatives, scientists, researchers, and young academics, many medical doctors participated in this year's event as they had the chance for intensive communication with the biomedical engineers.

One highlight of the day was the successful live knee surgery by Dr. Sandro Kohl, Senior Physician, Knee and Sports, Department of Orthopedic Surgery, Inselspital Bern. Illustrative explanations in the auditorium were given by Dr. Andreas Krüger, Senior Physician, Knee and Sports, Department of Orthopedic Surgery, Inselspital Bern.

At the end of the day, three awards for excellent academic achievements in the field of Biomedical Engineering at the University of Bern were presented.
Jonas Reber received the Medical Cluster Award 2012 for the best Master thesis for his work "Analyses of high-speed opto-biological data from excitable tissue".
The Medical Cluster Award 2012 for the best PhD thesis was given to Harald Studer for his work "Simulation of Refractive Surgery for Optimization of Vision Correction".
The SICAS Poster Award 2012 was given to Hadi Hosseini. His poster "Image-Guided Failure Analysis of Trabecular Bone under Large Compressive Strains" convinced the jury.



Harald Studer and Jonas Reber together with the president of the Medical Cluster, Rubino Mordasini.

Hadi Hosseini receives the SICAS Poster Award from the Director of the foundation, Bernhard Reber.

The Biomedical Engineering Club

The BME Club and Its Mission
The BME Club is an alumni club whose mandate is to promote networking among its interdisciplinary members. It connects you to a growing network of biomedical engineers, scientists, past and present students and medical technology corporates with a desire to bring together the principles of engineering, biology, and clinical medicine. These goals are accomplished by hosting events such as information sessions on the latest cutting-edge research in the fields of biomedical engineering, attending international conferences and touring various industrial plants and laboratories. The club is run by an executive committee following the dictates of our constitution, and it is recognized as an official alumni association of the University of Bern under the umbrella organization – Alumni UniBe.

We are an enthusiastic and versatile group with diverse activities:

- bi-monthly "Stammtisch" in a local restaurant to network, brainstorm or simply chat
- visits to medical and engineering companies
- providing information on career opportunities (job offers)
- organizing annual welcome event for "new students"
- organizing annual alumni meet
- participating in the annual BME day
- publishing the annual BME Newsletter
- providing access to Medical Cluster events
- joint membership with SSBE (Swiss Society for Biomedical Engineering)

BME Club Stammtisch at Restaurant Beaulieu in spring 2012.

BME alumni who join us will automatically become a member of Alumni UniBe, the alumni association of the University of Bern. Among other benefits this includes receiving a lifelong UniBe email address.
In short, the BME club represents a unique platform for professional lifelong communication and networking.
For further details look up our website at:
http://www.bmeclub.ch.

Executive Committee for 2011/2012
President: Prabitha Urwyler
Vice President: Tom de Bruyne
Secretary: Julia Spyra
Treasurer: Christian Güder
Webmaster: Tobias Imfeld
Faculty Representative: Dobrila Nesic
Master Students Representative: Lilibeth Salas Tellez
Alumni Representative: Lukas Bösch
PhD Students Representative: Matteo Fusaglia
Industry & Job Market Manager: Rudolf Sidler
Auditors: Lutz Nolte, Patrick Roth

How to Join
Becoming a member is easy! Simply sign up at any BME Club event or visit us at http://www.bmeclub.ch.

Grand Prix

May 13, 2012. Yesterday, we ran the GP Bern. It was super! I would recommend it to everyone who is willing to get a new feeling for the city and the culture. The city was wonderful, super alive, with music and people on every corner. Then at the Tierpark, a more mystic feeling, less noise and also allowing the runners to actually feel even closer to the other runners and to their own feelings. Over the course of the last kilometer, the whole effort was rewarded with a very warm ambience created by the people waiting for us. Despite pouring rain, despite an awfully wet spring day, they were supporting all the runners.

It was a fantastic experience. I enjoyed it very much, just like a child! The city was wunderschön, Bern – a magnificent scenery for such a run.

Juan Anso, BME student

The two BME Club teams (from left to right, from top to bottom): Matthias Peterhans, Patrick Roth, Christian Güder, Ishan Shah, Juan Anso, Daniel Lachner, Tom De Bruyne, Lukas Kohler.

Bowling

Late in November a group of alumni went bowling to the Marzili Bowling Center. The sneakers mounted, we started with the game on two lanes. Ball by ball is thrown against the pins and they have to stand up for many times on this evening. The time between the shots gave the opportunity to talk with your former classmates and an apéro, offered by the BME Club, satisfied the appetite. It was great to meet all of you. See you (and many others) at the next alumni event!

Lukas Bösch, BME alumnus

The bowling team (from left to right, from top to bottom): Thomas Sommer, Steffen Schumann, Kurt Gysi, Christian Güder, Lukas Bösch, Tobias Imfeld, Prabitha Urwyler, Lukas Kohler.

Graduation Ceremony

On March 24, 2012 the Medical Faculty of the University of Bern held their graduation ceremony at the Kultur Casino in Bern.

Together with their families and friends, the BME graduates celebrated their diplomas in a great and luxurious hall. The *Medizinerorchester* entertained the audience with musical intervals between the speeches.
After an enthusiastic speech by Prof. Dr. Benedikt Horn, the Biomedical Engineers received their master diplomas. For the first time, Prof. Zysset, the new program director of the Master's Program in Biomedical Engineering and follower of Prof. Nolte, handed the diplomas to the graduates.

This was the fifth graduation ceremony since the master's program had started in 2006.

Fatih Toy, BME alumnus

Program director Philippe Zysset with alumni Tom De Bruyne, Raphael Deschler, Timo Dietrich, Luaks Frei, Tobias Imfeld, Lukas Kohler, Daniel Lachner, Emmanuel Liechti, Yannick Lovis, Cherry Malonzo, Roger Mathys, Aymeric Niederhauser, Jonas Reber, Saloni Soin, Gregor Spreiter, Thomas Stübi, Fatih Toy, Andreas Treuholz, and Stefanie Uhl.

Graduate Profile

Iwan Eicher
Iwan Eicher graduated from the Master in Biomedical Engineering Program at the University of Bern in 2009.

BME: What was your academic and professional background prior to your BME studies?

IE: After primary and secondary school I did an apprenticeship as electronics engineer with the company Crypto AG in Steinhausen, Switzerland followed by an internship with the same company as a programmer for embedded microcontroller systems. During that time, I decided to continue my academic career and graduated three years later as Software Engineer FH after studying Computer Science at the University of Applied Sciences in Lucerne. Due to the fact that I was always interested in medicine I was very pleased to learn that it is possible to study BME at the University of Bern and I signed up for the master's program.

BME: Why did you choose to pursue your Master's studies at the University of Bern?

IE: The main reason was because the University of Bern offered a master's program in Biomedical Engineering with the possibility of working 40% part time as the courses were concentrated on three days. In addition, I assumed that Bern would be an ideal location to find a 40% part time job in the medical industry.

BME: You continued to work during your studies. How was this experience?

IE: I had a part time job as research assistant at the MEM Research Center (former ARTORG) and this was a great opportunity to connect and transfer the knowledge learned in the courses into real research projects. Thanks to these projects I made my first contacts with surgeons and other medical personnel at the University Hospital of Bern.

BME: What was your career plan after the completion of your degree?

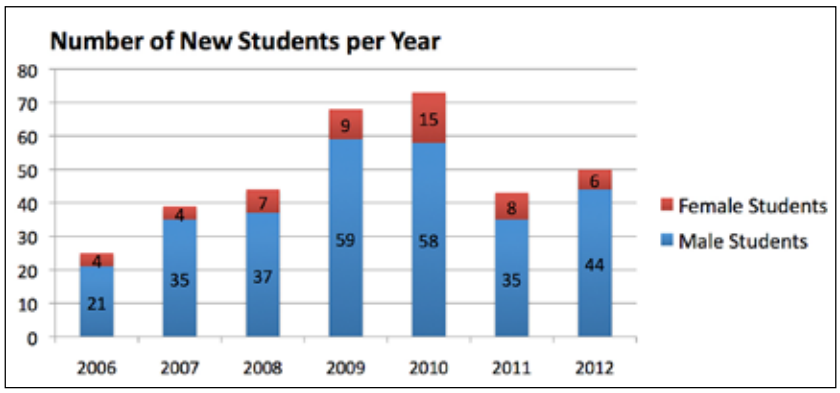
IE: After finishing my Master's thesis and graduating, I immediately applied for jobs in the medical industry. The combination of the thesis completed in the field of Ophthalmology and a Computer Science background made it possible to start as Software Engineer with the company Haag-Streit Diagnostics in Koeniz.

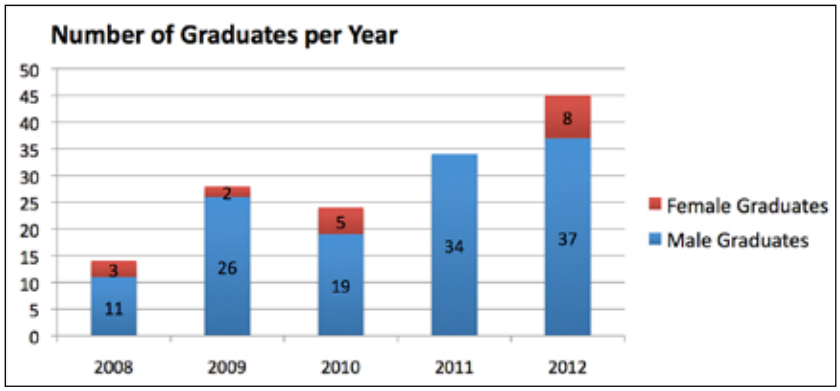
BME: What is the benefit of the Master studies with regard to your current professional activity?

IE: In my current position as Product Manager Perimetry I am the interface between our customers, research teams, key opinion leaders and the Research & Development team of Haag-Streit Diagnostics. On the one hand, this involves communicating with ophthalmologists and researchers, which requires a profound medical background to be accepted by these partners. On the other hand, a good knowledge in technical related disciplines (programming, statistics, regulatory affairs, etc.) is also necessary to interact with the Research and Development team or Competent Authorities.

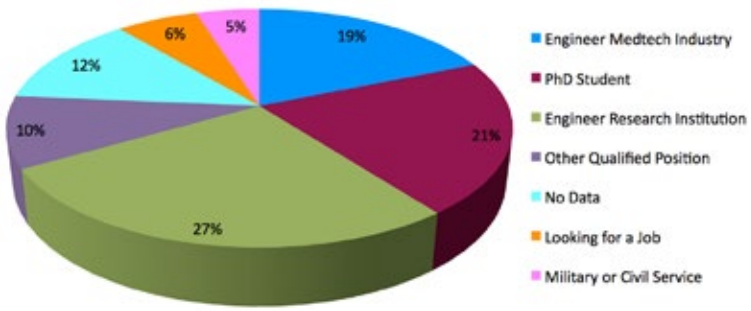
Statistics

Number of Students and Graduates per Year





BME Alumni: Career Directions
Profession after Graduation



Master Theses 2012

Please visit our website at http://www.bme.master.unibe.ch for an online version with full page Master Theses summaries.

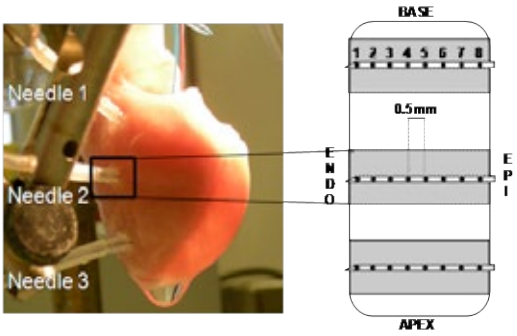
Analysis of Unipolar Electrograms and the Detection of the Arrhythmogenic Potential of Reference Drugs Recorded in a Langendorff Rabbit Heart Preparation

Christian Affolter

Supervisors: Prof. Dr. Andreas Stahel
Institutions: Bern University of Applied Sciences, Engineering and Information Techology
Examiners: Prof. Dr. Jan Kucera and Prof. Dr. Andreas Stahel

Background

The Safety Pharmalogy Department of Novartis investigates the influence of known torsadogenic drugs on a Langendorff in vitro rabbit heart preparation. In particular the transmural dispersion and the apico-basal dispersion of the repolarization wave as well the beat to beat variability of consecutive beats preceding Torsades de Pointes (TdP) is examined. In the experimental setup three needles, each containing 8 electrodes, are inserted in the left ventricular wall. After the atria is removed and the His-Bundle was cut, the heart is getting stimulated with an electrode placed in the ventricular septum where the His-Bundle is cut and the electrical propagation is recorded over these 24 electrodes.



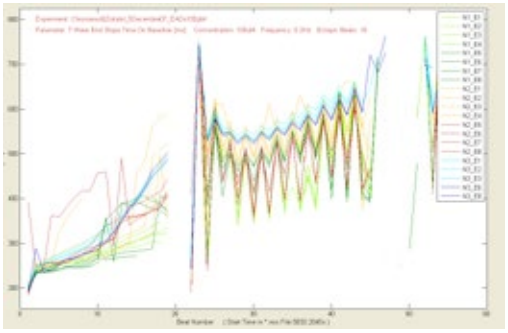
Rabbit Heart with Inserted Needles ; The Picture is Provided by Dr. Nicolas Guérard, Novartis Pharma

Project Scope

The goal of this thesis was to define and develop tools analyzing these recorded transmural electrograms. This signal analysis can be split up into two parts. On the one hand the filtering of the signal and on the other the parameter extraction of the electrocardiograms. The biggest challenge here was the detection of the parameters within the T-wave, because this repolarization phase can assume every possible shape.

Results

The new signal analysis of the recorded unipolar electrograms is the main part of this thesis. In addition a graphical user interface was generated to facilitate the statistical analysis of one or more experiments. Thanks to the new much more reliable signal analysis, the added parameters and the developed visualization tools, a much better basis for an eventual deeper pattern detection is realized.



Plot of the QT-Intervals of 60 consecutive beats before a TdP develops.

Discussion

Cause of the new closer look to the signals we know now that it is not possible to just look at sequences right before a TdP, then in most of the cases there are already so much ectopic beats around, that a detection of halfway reliable parameters is not possible. Another thing that one have to take into account with the 0.2 Hz sequence is that the steady state, after the pacing rate change from 1 Hz to 0.2 Hz is reached earliest after 30 beats and so it is not possible to look at more than 20 beats at steady state.

Crosslinking of Collagen Microcarriers for Expansion and Chondrogenic Differentiation of Mesenchymal Stem Cells

Fanny Oliveira Arcolino

Supervisors: Dr. Jivko Stoyanov
Institution: Swiss Paraplegic Research, Spinal Injury Research
Examiners: Prof. Dr. Benjamin Gantenbein and Dr. Jivko Stoyanov

Introduction

Back pain is a musculoskeletal disorder that affects 80% of the people at some point of their lives. Regenerative medicine and tissue engineering have goals to restore structure and function of damaged tissues and organs. We aimed to develop tissue engineering methods for intervertebral disc repair and specifically to crosslink cell culture surfaces as plastic or collagen microcarriers for expansion and chondrogenic differentiation of human mesenchymal stem cells (MSCs). In order to enhance cell attachment and produce a cost-effective cell culture solution, basic fibroblast growth factor (bFGF) was covalently immobilized on polystyrene cell culture surfaces via EDC/NHS crosslinker. Moreover, to provide local and direct stimulation of MSCs for proliferation and differentiation bFGF or transforming growth factor-β (TGF-β) were covalently immobilized on collagen microcarriers either by EDC/NHS or riboflavin/UV radiation crosslinking reagents.

Materials and Methods

MSCS were plated on non-modified polystyrene plate surfaces and on surfaces crosslinked with 1 or 2% of EDC/NHS in solution to evaluate improvement of cells attachment. MSCs were seeded on collagen microcarriers (positive and negative controls) and on collagen microcarriers crosslinked with growth factors (bFGF or TGF-β) by EDC/NHS or riboflavin/UV radiation crosslinker agents. MSC-microcarrier constructs were in culture for 3, 6 and 9 days for MSCs expansion and for 11 and 21 days for chondrogenic differentiation (Fig.1). Cell number and cell viability were measured by Trypan blue and Alamar Blue methods respectively. Chondrogenic differentiation was evaluated by gene expression of collagen type 1, 2 and aggrecan via qRT-PCR and extracellular matrix synthesis by immunohistochemical analysis.

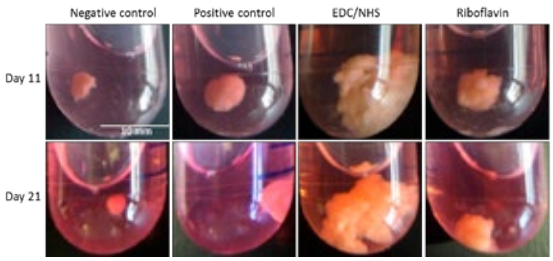


Fig. 1 MSC-microcarrier constructs after 11 and 21 days of chondrogenic differentiation. Initial cell number: 360'000. Negative control without TGF-β in the medium, positive control with TGF-β-containing medium, and EDC/NHS and Riboflavin are the agents used to covalently crosslink TGF-β on the microcarriers (medium without growth factor).

Results

Modification of polystyrene dishes via crosslinking of bFGF was a feasible way to reduce the use of growth factors for MSCs expansion, resulting in improved cell attachment and a less expensive cell culture. After nine days of proliferation on microcarriers, MSCs number was six times the initial on the positive control and on the microcarriers crosslinked with EDC/NHS or RF/UV radiation. Chondrogenic differentiation presented more synthesis of the extracellular matrix in the beginning of the culture for the microcarriers crosslinked with TGF-β, but was better for the positive after 21 days.

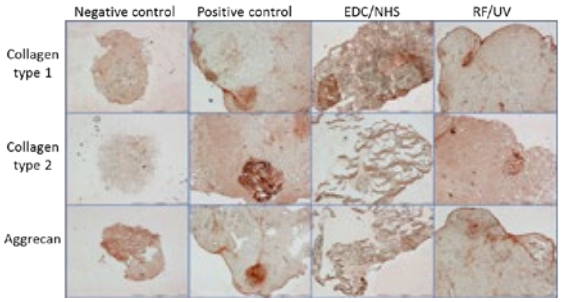


Fig.2 Immunohistochemical staining of MSC-microcarrier constructs after 21 days of chondrogenic differentiation. Collagen type 1, 2 and aggrecan in red-brown. Scale bar: 1000 µm.

Discussion

Expansion of MSCs on microcarriers crosslinked with bFGF corresponded to results of similar study performed with endothelial cells [1], proving to be a suitable method to stimulate cells proliferation using reduced amount of growth factors and acting only on the target cells. Avoidance of extended undesired stimuli may be important if translated into clinical practice of regenerative medicine, and bring us a step closer to a cost-effective cell-based therapy. Synthesis of extracellular matrix proteins on the crosslinked microcarriers was lower than the positive control probably because the TGF-β immobilized was consumed by the cells in the beginning of differentiation process, showing that cells need higher amounts of the growth factor for extracelullar matrix synthesis. EDC/NHS crosslinking prevented scaffold schrinkage during cells differentiation and provided a desirable repair device as tissue defect filler.

Reference

Wissink, M.J., *et al*. J Control Release, 2000. 67(2-3): p. 141-55.

Three-Dimensional Face Reconstruction From Video: Application to Aesthetic and Reconstructive Surgery

Christian Baumberger

Supervisors: Dr. Thiago Oliveira dos Santos and Dr. Mauricio Reyes
Institutes: Institute for Surgical Technology & Biomechanics, Universität Bern
Examiners: Dr. Mauricio Reyes and. Dr. Marcel Lüthi

Introduction

The human face is a vital component of our identity and along with its functional aspects it provides us with many intricate and complex communication channels to society. Aesthetic plastic surgery plays a major role in today's society. It involves techniques like Rhinoplasty or Chin augmentation intended to enhance the appearance through surgical procedures. To this end, surgeons rely on illustrations, other patient's photographs, 2D computer animations, or complex and cumbersome 3D-laser technologies as a communication and preoperative planning tool. Recently, a photogrammetric-based system, which relies on one frontal and two lateral images, has been proposed as a simple and hardware-free tool for planning aesthetic procedures as well as communicating with the patient. However, accuracy of the 3D face representation in certain regions is compromised due to the lack of information contained in only three images. To overcome this drawback, this thesis proposes an alternative solution to create a 3D face representation of the patient based on a video generated within a clinical scenario.

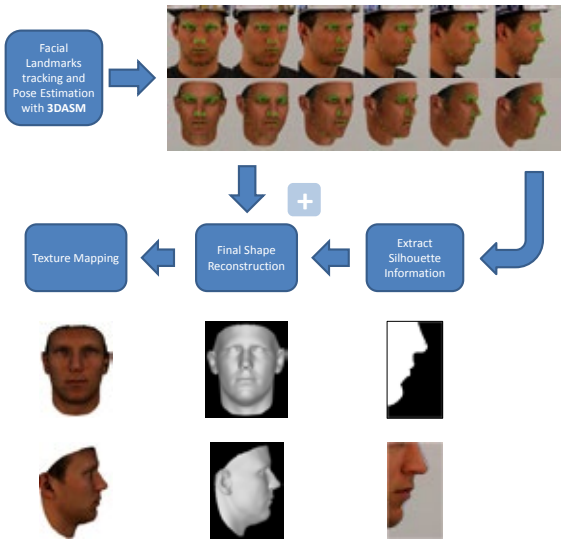


Fig. 1 Overview of the 3D Face Modeling Algorithm

Materials and Methods

The application models the patient's face based on the full video sequence with a minimal Doctor-Application interaction. The proposed 3D face modeling algorithm incorporates internal facial landmarks in combination with silhouette information and iteratively adapts the facial shape to best represent the facial structure contained in the frames of the video sequence (see Fig. 1). A new presented 3D active shape model enables the spatio-temporal tracking of facial landmarks and estimates the face pose for each individual frame after a manual initialization of certain facial landmarks at the beginning of the sequence. In order to establish a realistic 3D model, facial texture is extracted from selected key-frames and is projected to the 3D shape in a seamless way. For evaluation purposes, we recorded video and 3D-scan data of 20 subjects wearing an in-house designed calibration helmet. The data was subsequently used to automatically generate ground truth data for evaluation of pose estimation, landmark detection and 3D reconstruction.

Results and Discussion

3D face modeling including landmark detection, pose estimation and 3D shape estimation was performed for each of 20 real cases and 20 artificially generated cases and compared to the ground truth. The results showed that the proposed 3D active shape model can be used to detect facial landmarks with an approximate median error of 5 percent intraocular distance and a pose estimation median error for roll, pitch and yaw angle below 5°. Qualitative analysis showed problems to accurately detect facial landmarks in the mouth and eyes region, but it also showed that it does not significantly affect the overall 3D face modeling. By incorporating silhouette information into the 3D face modeling algorithm, all facial regions (eyes, nose, mouth and cheek plus chin) experienced an increase in modeling accuracy. The cheeks-chin region showed the largest improvement. In general, the results showed an improvement on the 3D face modeling accuracy with a video based approach, especially in regions where the photogrammetric three images based system lacks information. Furthermore, the rigid pose assumption of the photogrammetric-based system could be alleviated with the presented method for facial pose estimation.

Acknowledgements

KTI Promotion Agency (grant: 12892.1 PFLS-LS).

Intracorporeal Energy Harvesting from Arterial Deformation

Mohamed Ben Messaoud

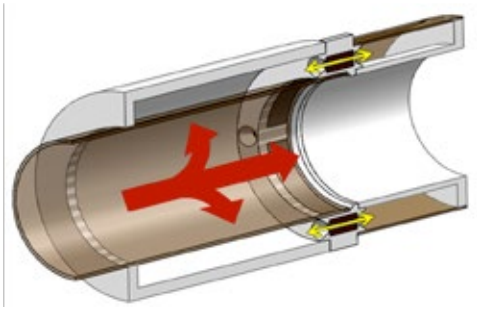
Supervisors: Aloïs Pfenniger
Institutions: ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Rolf Vogel and Prof. Dr. Stijn Vandenberghe

Background

Various implantable devices such as pacemakers, defibrillators, or neuro-stimulators require some sort of electrical power supply, which is usually realized by internal primary batteries. The major limitation of this reliable energy source is the need for complete device replacement after battery discharge. Rechargeable batteries are not employed since they are inferior with respect to device safety and energy density. External batteries in conjunction with percutaneous power cables have potential complications such as infections and cable fractures.

Project Scope

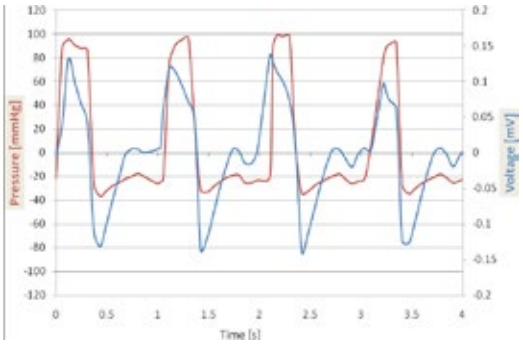
A magnetohydrodynamic (MHD) generator that harvests energy from the arterial wall deformation was designed and mathematically evaluated in the ARTORG Cardiovascular Engineering research group. Outside the artery, an electro-conductive fluid is propelled by the motion of the arterial wall from a first chamber to a second chamber through small ducts (cf. figure below). In the presence of a magnetic field, the kinetic energy of the fluid is converted into electrical energy. The aim of this master thesis is to develop and test a prototype to evaluate this concept.



3D CAD model of the Magnetohydrodynamic generator intended to harvest energy from the arterial wall deformation.

Development

Gallium alloy performance as electro-conductive and low-melting point fluid was investigated. As a result, it showed very interesting electric conductivity and viscosity. To simulate the elasticity of vessels, natural rubber latex tubes were utilized, due to their very low modulus of elasticity. These tubes were fabricated by dip-coating process. A part that was fabricated by rapid prototyping contains four small ducts connects the two chambers. After that, permanent magnets were placed between the ducts to produce a magnetic field perpendicular to the axis of the duct. Finally, the different components were assembled with respect to the most important requirement of the design.



Produced voltage compared to the pressure inside the elastic tube.

Results and Conclusion

The measured output voltage showed relatively close values to the ones predicted by the simulation. This proves the ability of the prototype to harvest energy form the arterial deformation.

For the future, an improved prototype of the MHD generator will be constructed to allow more accurate testing and comparison.

Voxel-based Thickness Measurement of the Neonatal Human Cerebral Cortex in Magnetic Resonance Images

Tobia Brusa

Supervisors: Prof. Dr. Philippe C. Cattin
Institutes: Medical Image Analysis Center (MIAC) in collaboration with the University Children's Hospital,Pediatric Radiology, Basel
Examiners: Prof. Dr. Philippe C. Cattin and Prof. Dr. Med. Till Sprenger

Introduction

Even though the cerebral cortex is by far the largest partition of the human nervous system, little is known about the development process from the immature brain to the mature brain. The cerebral cortex is the sheet-like rim, called gray matter (GM), consisting of billions of neurons. It is highly folded, covers the white matter (WM) core, and lies inside the cerebrospinal fluid (CSF). Macroscopically, the cortex is structured into folded gyri pointing outward and folded sulci looking inward. On the large scale it is separated into two hemispheres.

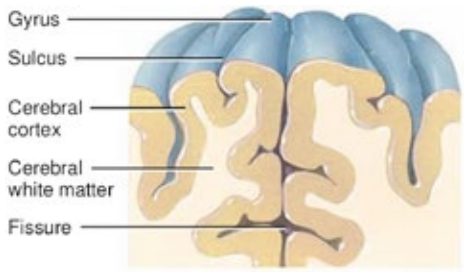


Figure 1: Details of a gyrus, sulcus, and fissure. (Image source: Principles of Anatomy and Physiology, 12th Edition)

The study of the brain morphology, the thickness of the cerebral cortex to be more precise, during development is a challenging task. This is due to insufficient MR-acquired image quality. Accountable for the low image quality during this time span are mainly (1) the poor spatial resolution, (2) the low and changing tissue contrast, and (3) a high within tissue intensity variability.

Methods

Our goal is the volumetric analysis of the cortical ribbon. Prior to it the cerebrum extraction, also known as skull stripping, and the tissue differentiation of brain images between GM, WM, and CSF is required. The cerebrum extraction process and the segmentation step are based on the Infant Brain Extraction and Analysis Toolbox (iBEAT). For the thickness calculation of the cortex, on the other hand, a novel voxel based approach has been developed. It consists of (1) a Euclidean distance transform, (2) a spatial crest line extraction, and a thickness calculation over an arithmetic mean of the extracted crest line values. It is worth mentioning that the introduced method to extract the crest line has a nice side-effect - it can not only be used for MR images of neonates but for any kind of labeled 3D objects.

Results and Discussion

The implemented workflow makes the measurements of the cortex thicknesses in MR images of newborn infants feasible. The results in experiments with synthetically generated data sets are promising. Furthermore, the analyses of the measured thicknesses on six data sets of neonates acquired at the University Children's Hospital in Basel have shown reliable and realistic results. Although, the implemented workflow and the novel cortical thickness measuring method showed encouraging results further development and research is needed. Specifically, the introduction of sub-voxel accuracy in the thickness measurements and statistical analysis of the workflow based on the manual extraction of the cortical thickness in many brain regions. However, in vivo imaging technology is also advancing rapidly, allowing sufficiently high resolution and high tissue contrast in the near future.

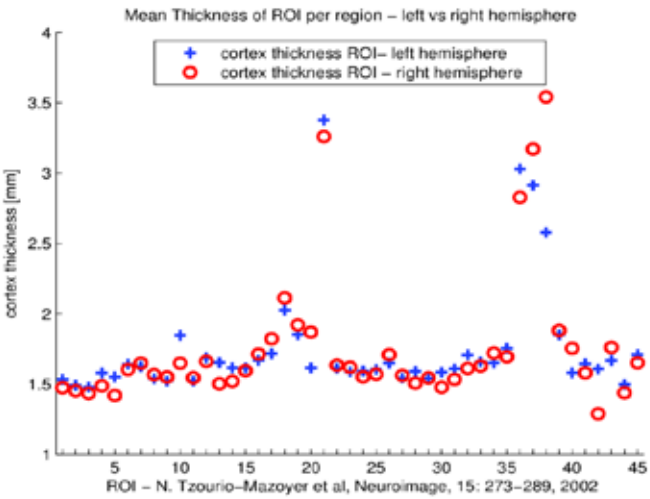


Figure 2: The calculated cortex thicknesses per region according to the parcellation map introduced by Tzourio-Mazoyer et al. for the left (blue, +) and right (red, o) hemisphere.

Konzeptionierung und Realisierung einer Vorrichtung zur produktionseffizienten mechanischen Konditionierung der Innenoberflächen von selbstexpandierenden Stents für die unteren Extremitäten

Biagio-Roberto Cammarano

Supervisors: Dr. Sebastian Klaus
Institutions: Eucatech AG, Leitung Forschung und Entwicklung
Examiners: Prof. Dr. Rolf Vogel and Prof. Dr. Stijn Vandenberghe

Einleitung / Aufgabenstellung

Die periphere arterielle Verschlusskrankheit (pAVK) beschreibt eine Störung der arteriellen Blutperfusion der oberen und v. a. der unteren Extremitäten. Hervorgerufen wird diese durch den Vorgang der Arteriosklerose. Um die Blut-perfusion wiederherzustellen können in einem minimalinvasiven Verfahren die Ablagerungen mittels einem Ballon-Katheter in die Gefäß-wand eingedrückt und das Gefäß in diesem Bereich mittels eines Stents dauerhaft mecha-nisch gestützt werden. Diese Stents können aus einer Nickel-Titan-Legierung hergestellt sein, die als Nitinol bezeichnet und durch ihr super-elastisches Verhalten den biomechanischen Anforderungen gerecht wird. Aufgabe dieser Arbeit ist es, den aktuellen Prozess der Stent-Fertigung zu untersuchen und Lösungen für eine Optimierung der Innenoberfläche der Stents zu finden und die Produktionseffizienz zu steigern.

Vorgehensweise

Um das Ziel der Arbeit erfolgreich umzusetzen wurde in einem ersten Schritt der aktuelle Serienprozess analysiert. Nach der Analyse wurde ein Lastenheft erstellt, das Anforde-rungen an eine künftige Anlage und damit ver-bunden an eine Prozessabfolge enthält. An-hand von Screening-Versuchen wurden auf dieser Basis diverse Optimierungsmöglich-keiten für die bisherigen Prozessschritte unter-sucht. Aufgrund der Ergebnisse aus den Screening-Versuchen wurde wiederum ein Pflichtenheft erstellt, eine Anlage angeschafft, Hilfsmittel realisiert und eine neue Prozess-abfolge definiert. Diese wurde daraufhin auf eine mögliche Serieneignung untersucht.

Ergebnisse

Nach Abschluss aller Untersuchungen lässt sich zusammenfassen, dass eine Kombination zwischen Anlage und Prozessabfolge gefunden wurde, durch die eine Optimierung der Ender-gebnisse und eine verbesserte Reproduzier-barkeit sichergestellt sind.

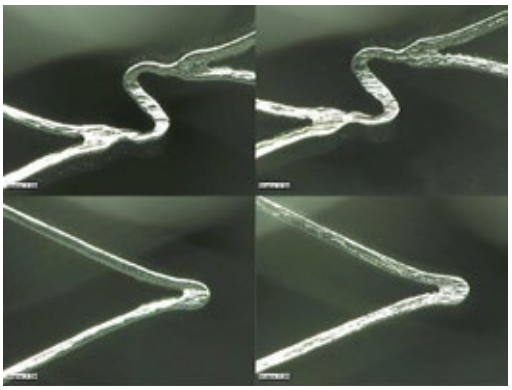


Abbildung 1: Endergebnisse nach neuer Prozess-abfolge (links) und Endergebnisse nach bisherigen Serienprozess (rechts) (Vergrößerung 200-fach)

Ausblick

Für eine Serieneinführung sollten die Hilfs-mittel gemäß dem Pflichtenheft angepasst wer-den. Im Anschluss daran kann eine Prozess-validierung durchgeführt werden. Eine zu-sätzliche Untersuchung der neu prozessierten Stents auf mechanische Eigenschaften ist vor-zunehmen. Bei einer erfolgreichen Umsetzung der genannten Punkte kann diese Arbeit als Grundlage für einen künftigen Serienprozess angesehen werden. Durch die Einführung einer entsprechenden Prozessabfolge wird eine nachhaltige Steigerung der Produktions-effizienz realisiert.

Wireless Functional Electrical Stimulation

Adrian Derungs

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Institutions: Institute for Rehabilitation and Performance Technology, Bern University of Applied Sciences
Examiners: Prof. Dr. Kenneth J. Hunt, Prof. Dr. Tobias Nef

Introduction

Functional Electrical Stimulation (FES) provides various approaches for rehabilitation for patients who suffer paraplegia or stroke. FES allows restoring and maintaining motion and Activities of Daily Living (ADL) can be performed. This gives disabled people the opportunity for independence. These facts served as the motivation to implement a novel wireless device for FES. The aim of this project was the development of a complete system to demonstrate the feasibility of wireless stimulation with four channels.

Materials and Methods

The wireless FES system consists of two stimulators to apply the stimulation with four channels and one coordinator to control the stimulators. The stimulator was supplied by a 7.4 V Li-Po battery and enclosed in a 70 × 52 × 35 mm portable case fitted with a belt. The stimulator was voltage regulated and capable of producing biphasic pulses. An Atmega328 microcontroller from Arduino was used. To transmit data, Bluetooth modules Bluetooth Mate Silver from Sparkfun and BGB203 from Olimex were connected with the microcontroller. To indicate communication and stimulation, status LEDs were mounted. For stimulation, surface electrodes from Danel Healthcare were used, connected to the stimulator via USB basis for the coordinator was the Evaluation Board MCBSTM32EXL from Keil.
The stimulator algorithm interpreted received data and generates desired pulses. Several modes were programmed to select the number of activated channels and pulse patterns. The pattern was defined by variables *Mode*, *Pulsewidth*, *InterPulsetime*, *RestOfperiod*, *Repetitions*, *Drift* and *OverallRepetitions*. The coordinator run with a Real Time Operating System (RTOS) and allowed Bluetooth setup and parameter adjustment via joystick.

Results

A prototype for wireless stimulation with four channels was developed. Bluetooth had a range of 45 m indoors. The booster output voltage was reliable and stable. The deviation to calculated output voltage was 2.2 % for the stimulator with 30 V and 1.2 % for the stimulator with 50 V. The modulation time of signals with respect to baud rate was calculated to be maximally of 2.2 % with respect to measured modulation time. It was demonstrated that latency for data transmission was 16.82 ms, 20.57 ms and 41.76 ms by baud rates of 115200 Baud, 57600 Baud, and 9600 Baud respectively. Stimulation was as expected for different loads. For a pure resistive load the current follows the adjusted biphasic rectangular shape. For loads with capacitive elements the current had an exponentially decreasing shape. 20 % of adjusted parameters had larger deviation than the specified 10 %. The material cost for the prototype, including the coordinator and two stimulators, was 715 SFr.

Figure 1 30 V Stimulator providing two channels. Bluetooth module (red) microcontroller (blue).

Discussion

The objective of a mobile stimulation with four channels was fulfilled. The measured output voltage of the booster corresponded with the calculation as stated in the datasheet. The required time for data modulation could be determined by calculation and coincided with measurements. Handling of Bluetooth latency is a challenge for further development since it was not constant. The resulting waveforms through different loads can be explained by principles of electrical engineering. The costs are acceptable.

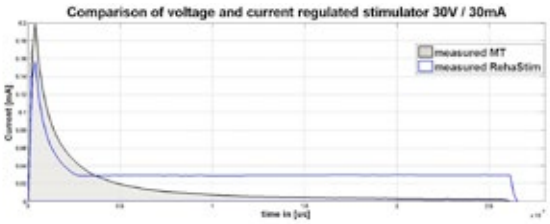


Figure 2 Comparison of the amount of charge generated by a voltage- (grey) and current regulated (white) stimulation.

Acknowledgements

Prof. Dr. Kenneth J. Hunt and the Institute for Rehabilitation and Performance Technology

Development of an Osteosynthesis Plate to Treat Distal Radius Fractures from Dorsal

Timo Dietrich

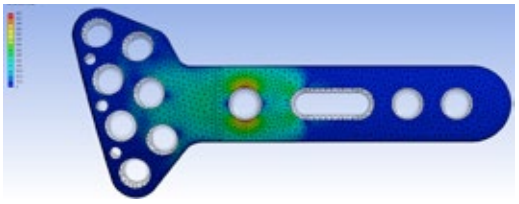
Supervisors: Dipl. Ing. Philip Henry
Institutions: Stryker Osteosynthesis, SonicFusion
Examiners: Prof. Dr.–Ing. Lutz Nolte and PD. Dr. Philippe Büchler

Background

The distal radius fracture is known as the most common fracture in humans. The most common reason for distal radius fractures is falling from a standing position onto the outstretched hand. As the bone quality decreases and the risk of falling increases in older people, the fracture risk for this group is especially high. According to other fracture types it is expected that the incidence of distal radius fractures will continue to rise in the future. Actual the volar plate osteosynthesis is the golden standard of distal radius fracture treatment. Since it is possible to fix dorsal bone fragments with locking screws from volar, the popularity of the dorsal approach decreased. Because of missing muscular coverage on the dorsal side of the radius, these implants tend to irritate the tendons which slide above them. Nevertheless the dorsal approach has also advantages and makes still sense in certain situations.

Project Scope

Part of this project was to compare these two types of plate osteosynthesis on the basis of current literature. Finite Element Analysis was used to investigate the stability of the Stryker implants and their behavior in the event of applied load. Based on these results and the findings from literature research a profile of requirements was defined, which should help to increase the implant stability and decrease tendon irritation problems. Goal of the project was the implementation of these requirements to a design for a new plate generation for dorsal distal radius plates.



ANSYS simulations were used to determine the Von-Mises stress distribution in the implants.

Results

Based on the FEA simulations a plate design with a higher stability was developed for the actual Stryker plate generation. Furthermore concepts for a new generation of a dorsal distal radius plate were developed and implemented to a CAD model.

CAD model prototype of the new generation plate for dorsal treatment of distal radius fractures.

Discussion

The FEA results correspond to findings of studies which state that unfilled screw holes increase the risk of plate failure. The performance of the new plate generation according to tendon irritations has to be investigated by further in-vitro tests.

Development of a Novel Device for Trunk Muscle Activation Using Stochastic Resonance

Patric Eichelberger

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Applied R&D Physiotherapy, Bern University of Applied Sciences
Examiners: Prof. Dr. Volker M. Koch and Prof. Dr. Lorenz Radlinger

Introduction

Back pain is a very common and cost intensive concern that is present in today's society. The growth in incidence rate is often attributed to an increasingly unhealthy lifestyle. Recent studies propose stochastic whole body vibration exercise as an efficient method to treat back pain. Further research is necessary to better understand the mechanisms. Many commercial devices enabling whole body vibration training are already available today, but only few provide stochastic motion patterns. Furthermore, none of these allow to set up exactly defined stimulation patterns. Yet, the precise control over the stimulation pattern is crucial for a profound and systematic research in the field. Therefore, a novel device addressing those needs is required.

Materials and Methods

Requirements for a new research device that is able to activate the trunk muscles of the human body with mechanical whole body stimuli were defined. The most important point was to find the necessary degrees of freedom. The main challenge was to define the term *optimal stimulation*. Therefore, a profound literature research was performed and findings were discussed with an expert. The kinematics is designed in relation to the functional anatomy of the trunk muscles and it was found that stimulation must be applied over three rotational degrees of freedom. An input-output analysis brought out the system concept shown in figure 1.

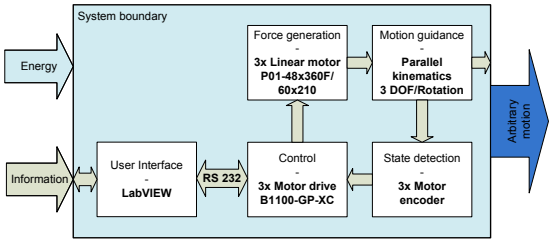

Figure 1: System concept with LabVIEW as software solution and a parallel kinematic mechanism providing three rotational degrees of freedom, actuated by linear motors.

To estimate the loading conditions a body model based on anthropometric data was developed. The system was specified during the detailed study, which included calculations, definition of mechanical and electrical setup as well as the development of software and user interface.

Results

A functional prototype was developed based on which the functionality could be proven. The device provides a range of motion of +/- 13° around each of the three rotation axes. The parallel kinematics together with the linear motors leads to low internal inertia and therefore permits high accelerations. Amplitudes larger than 1° can be generated with frequencies of up to 15 Hz. The prototype allows to set up arbitrary rotation axes and to perform harmonic oscillations around them. Stochastic motion can be introduced through random variation of frequency, amplitude or rotation axis.

Discussion

The current development provides a new and unique research tool to any researcher interested in the interaction between human and mechanical whole body stimuli. The new system offers a stimuli generation dependent on the research needs. Researchers do not have to rely on commercial devices anymore that offer only a limited range of oscillation settings. Through its flexible stimulation patterns, our system enables a broader research that aims to better understand the effects of mechanical whole body stimuli onto the human. We expect that the effectiveness of stochastic whole body vibration for reducing back pain can be proven in the future and that in this way the current development helps people suffering from back pain.

Acknowledgements

The project was supported by the Institute for Sport Sciences, University of Bern and from the two industry partners idiag AG and Girsberger AG. Their contribution is gratefully acknowledged.

Life Saving Robot for Elderly People

Lukas Frei

Supervisors: Prof. Dr. Volker M. Koch
Institutions: Bern University of Applied Sciences, Engineering and Information Technology
Examiners: Prof. Dr. Volker M. Koch and Prof. Dr. Elham Firouzi

Background

Elderly people often suffer from isolation and fear to have a serious problem when being alone at home. One hard fall, a hypoglycemic coma or a stroke may cause the person to die because nobody is there to help.

The goal of this project is to build a prototype robot which can accompany his owner and detect physiological anomaly. If a problem has been detected, the robot can send an alarm to one or more trusted people to ask for help. The robot can then be remotely-operated from a PC or Smartphone, such that the alarmed person can check what happened.

Fig.1, A first prototype of a self balancing autonomous robot with a low power PC, a microcontroller for real time processing and many sensors.

Project Scope

The aim of the project is to build a mobile platform that can navigate autonomously through an apartment, as well as be remotely steered over the internet with a webcam. A web server is used to display all medical information on a website and to steer the robot. Medical sensors are used to measure physiological data and an algorithm is implemented to detect anomaly. And an estimation of the cost of the robot in case of industrial production is done.

Results

Costs for the material used in the construction of the actual prototype amounts to about 1000 Swiss francs. Further improvements of the prototype combined with the advantage of mass production can reduce these costs to at most 600 Swiss francs. This does not take into account the medical sensors. The robot needs to be developed further and tested in real conditions before a commercial use can be started.

Fig.2, The bioharness from Zephyr is a chest belt which measures the heart rate, breathing rate, movements and body temperature. It sends this information to the robot over Bluetooth. Source: Zephyr-technology.

Discussion

This project can be the starting point of a bigger project with the aim of developing a commercial product. To achieve this, an industrial partner should be found.

Development of an Enzyme-Driven Intervertebral Disc Degeneration Model

Tina Furtwängler

Supervisor: Prof. Dr. Benjamin Gantenbein-Ritter
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Center of Applied Biotechnology and Molecular Medicine, University of Zurich, Switzerland
Examiners: Prof. Dr. Benjamin Gantenbein-Ritter and Dr. Peter J. Richards

Introduction

Intervertebral disc degeneration (IDD) shows a balance shift from anabolic towards catabolic enzymes. This study aimed to develop a model of enzyme-driven IDD using bovine coccygeal intervertebral discs (IVDs) to mimic the clinical outcome of IDD in humans. This model could be used for investigation of therapeutic treatment options and may also partially replace *in vivo* animal models. The hypothesis implies that injection of exogenous MMP-3, ADAMTS-4 and HTRA1 in the center of the nucleus pulposus (NP) of an organ culture model would create similar damage as seen in human IDD.

Materials and Methods

Five IVDs were harvested from calf tails aged 6-9 months maintaining the endplate. MMP-3, ADAMTS-4 and HTRA1 were injected into the NPs of three discs, each at a dose of 10µg/ml and phosphate buffered saline (PBS) as a control into the fourth disc. A fifth disc served as day 0 control. Injected discs were cultured for 8 days, including a period of diurnal loading (0.4MPa) from day 1 to day 4 using custom-made specimen chambers. This experimental setup has been repeated five times (n=5).

Fig. 1 Loaded IVDs in custom-made chambers in 37°C incubator at 5% CO_2. Disc were previously injected with MMP-3, ADAMTS-4 and HTRA1 and PBS as a control and cultured for 8 days with a period of diurnal loading (0.4MPa for 16h, no load for 8h).

Outcome parameters included disc height, metabolic cell activity, DNA and glycosaminoglycan (GAG) content, and the expression of anabolic and catabolic genes, evaluated by real time PCR.

Results

The mean metabolic cell activity in the NP area was significantly lower in discs injected with ADAMTS-4 than in day 0 controls (p=0.0433), which is a feature of IDD. Change in disc height and GAG content as well as the DNA content did not show significant differences amongst the groups. Expression of MMP-13 was significantly higher in AF tissue of the PBS control group than in the group injected with MMP-3 (p=0.0227).

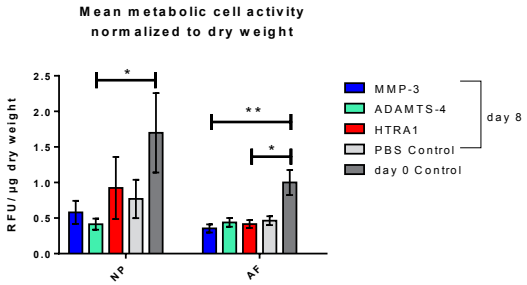

Fig. 2 Mean metabolic cell activity of injected samples cultured for 8 days and of day 0 control group. RFU values were normalized to dry weight. Significant differences could be found in the NP: ADAMTS-4 vs. day 0 group: p=0.0433 and in the AF: MMP-3 vs. day 0 (p=0.0079) and HTRA1 vs. day 0 (p=0.0349).

Discussion

The results suggest that ADAMTS-4 could provoke signs of IDD and might be suitable for the enzyme-driven model. MMP-3 and HTRA1 as well as the influence of different loading conditions, incubation time and enzyme concentration should be further evaluated. Understanding the pathways in more detail is of great importance for investigation of future therapies for IDD.

Acknowledgements

Grateful acknowledgement to the whole group of Tissue & Organ Mechanobiology, namely Benjamin Gantenbein-Ritter, Samantha Chan, Elena Callandriello and Azadeh Kabiri for their help and support. Many thanks also to Peter Richards for providing the HTRA1 enzyme.

Development of Hardware for Impedance Spectroscopic Assessment of Stent-Artery Systems

Samuel Gerster

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Institutions: Bern University of Applied Sciences, Engineering and Information Technology
Examiners: Prof. Dr. Rolf Vogel and Prof. Dr. Josef Götte

Background

Stent implantation is a surgical intervention for the treatment of coronary diseases. Possibly deadly complications can arise if the organism rejects the stent by growing scar tissue over it or if the stent is not incorporated at all in the endothelial layers and clots form on it. Methods exist for the measurement of endothelialization, but they lack resolution.

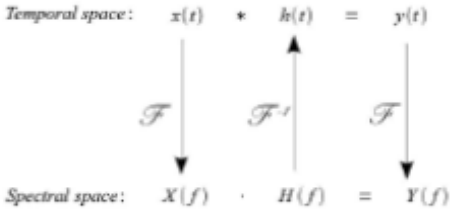
The aim of this project was to develop a system that would allow a precise diagnosis of the stent with a surgical intervention similar to the implantation of the stent. The endothelialization level can then determined through impedance spectroscopy.

Method

In order to perform the electrochemical impedance spectroscopy (EIS) two methods where analyzed, but both have the same basic principle: apply a current and measure a voltage drop across a certain amount of substance. The substance can then be identified through the characteristic impedance over a frequency range.

The first method, single frequency EIS, consists in applying a single frequency signal on the sample, perform the measurement and start over at a different frequency. Repeated often enough, this method yields a full spectrum of the sample's characteristic impedance.

The point of the second method, FT-EIS, is to obtain the full spectrum through a single measurement, injecting a multiple frequencies signal (X(F)) and analyzing the result (Y(F)/ X(F)) through a Fourier transform.

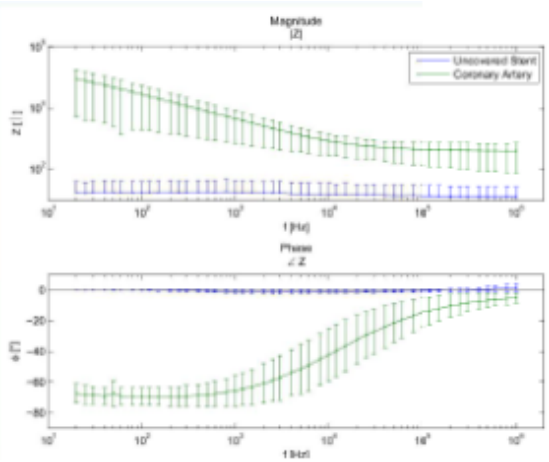


Both methods where tested for differentiation capabilities of fixated coronary artery tissue and uncovered stents.

References

[1] Tim Siiselbeck et a! In vivo intravascular electric impedance spectroscopy using a new catheter with integrated microelectrodes. In Basic Research in Cardiology 100(1):28- 34, 2005

Results



Both methods yielded good results over nearly the full specter (20-1MHz). The picture above shows the result obtained through the first method and indicates that impedance magnitudes can be told apart on the complete spectrum whereas the phase is indistinguishable around 1 MHz.

A hardware was outlined for future projects. It was designed for FT-EIS because this method yielded much better acquisition time and the (acquisition) hardware requirements are about the same. Even though the present results are not perfect, FT-EIS also promises much more detailed results for a comparable acquisition time.

Discussion

Some similar research has been done by Siiselbeck et al [1]. However, there are some key differences to our work. Even though [1] covered the complete spectrum, they chose to isolate one frequency at which they knew they could differentiate the impedance of the stent and the impedance of the endothelial tissue. They then observed the tissue growth over time and discovered a significant difference between the readings for the freshly implanted stent and the measurements after a few weeks.

Our method uses the full spectrum for the differentiation. Also it introduces FT-EIS in this field, reducing considerably the measurement time, allowing a full spectrum measurement in the first place. Furthermore it uses both magnitude and phase for the differentiation.

Remote Control of Insulin Pump: An Android Based Approach

Raphael Gränicher

Supervisors: Prof. Dr. Stavroula Mougiakakou
Institutions: ARTORG Center for Biomedical Engineering Research, Diabetes Technology Group
Examiners: Prof. Dr. Stavroula Mougiakakou and Prof. Dr. med. Peter Diem

Background

Diabetes mellitus is a chronic disease caused by the disability of the human body to produce the insulin adequately. This dysfunction leads to fluctuation of blood glucose concentration out of normal range. Uncontrolled diabetes can cause serious short-term (acute), e.g. hypoglycemic and hyperglycemic events, and long-term (chronic) complications, e.g. heart diseases, neuropathies, nephropathies etc. World Health Organization (WHO) estimates that more than 346 million people worldwide have diabetes, while this number is likely to be more than double by 2030.

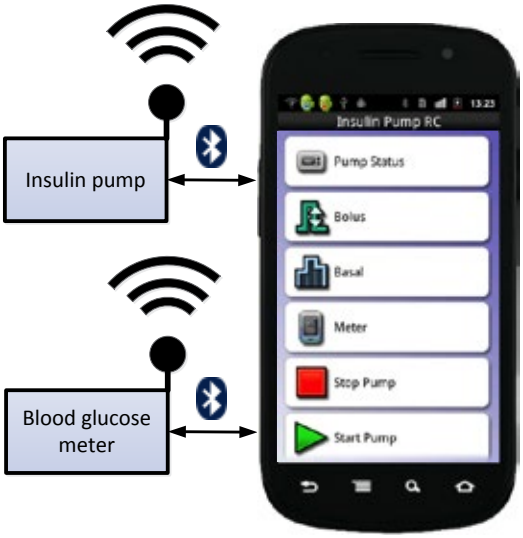
Glycemic control involves i) regular self-monitoring of glucose levels using either blood glucose meters or continuous glucose monitors and ii) external insulin intake either via multiple daily insulin injections or via subcutaneous insulin infusions (insulin pumps).

Project Scope

The aim of this MSc Thesis was to develop an Android based mobile phone application for the wireless control of a novel insulin pump. The application was designed for Type 1 diabetic patients who are using a novel insulin pump and a novel blood glucose meter without display. Ultimate goal is the enhancement of diabetes self-management.

Using the Bluetooth communication link the mobile phone application controls the novel pump and displays information from the novel blood glucose meter. Specifically, basic pump functionalities related to insulin treatment are accessible to be modified and adjusted by the smartphone. Furthermore, important pump data can be sent electronically from the mobile phone application to the treating physician or to the patient, in order to monitor the status of the disease and assess the effect of the followed diabetes treatment. User friendly interfaces have been developed for the handy monitor of insulin treatment and blood glucose concentrations by the diabetic patient.

During the MSc thesis emphasis was given to safety and security issues. A safety concept was developed based on literature review and regulatory requirements in order to protect the patient from any hazards. Security issues were treated in a more theoretical approach. Specifically, technical vulnerabilities related to the Android platform and the Bluetooth communication link were identified and analyzed. Finally, technical countermeasures that mitigate the security risks are presented.



System scope, Insulin pump and blood glucose meter connected to Android smartphone by Bluetooth communication

Discussion

Based on the penetration of mobile phones and the indications that insulin pumps improve diabetes control, the developed mobile phone application accompanied by the safety and security concept might be a promising approach towards enhanced diabetes self-management.

Periodicity Analysis of the Electrocardiogram (ECG) in Epilepsy Patients

Christian Güder

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Institutions: University Hospital Bern, Inselspital,
Universitätsinstitut für Diagnostische und Interventionelle Neuroradiologie
Examiners: Prof. Dr. Rolf Vogel and PD. Dr. Kaspar Schindler

Clinical background
Epilepsy is the second most frequent neuro- logical disease, affecting about 80.000 patients in Switzerland. Recurrent epileptic seizures are associated with increased mortality, whose main reason is sudden unexpected death of epilepsy patients (SUDEP).

Its cause is still debated but seizure associated cardiac arrhythmias offers one explanation. A current hypothesis is a disturbance of the central regulation of the autonomic nervous system that predisposes epilepsy patients to cardiac arrhythmias.

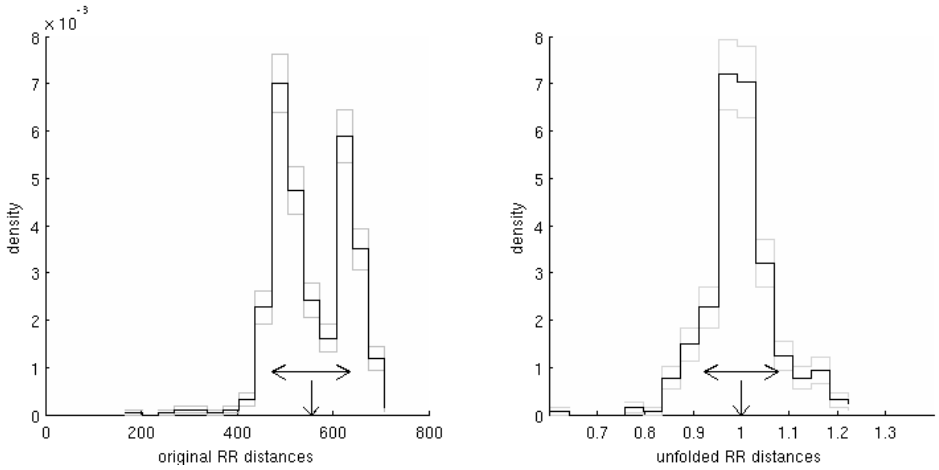
Project Scope
100 seizures from 15 patients taking part in the epilepsy program of the Inselspital were examined using long-term video-EEG together with a single lead ECG. The heart rate variability (HRV) assessed through RR intervals was dependent on conditions such as breathing rate or level of physical activity.

The “unfolding” procedure originally developed in Random Matrix Theory (RMT) was applied to extract trends while conserving the statistical properties of fluctuations. In pieces of pre- and postictal ECG segments of three minutes duration, correlations between consecutive RR intervals were quantified using currently used HRV measures. Additionally the short- and long-range correlations in the heart beat sequences were quantified using RMT measures.

Results
It was demonstrated that unfolding may indeed improve HRV analysis. Situations with abrupt heart rate changes make mean RR duration and standard deviation bad descriptors of HRV. After unfolding bimodal histograms of such RR distances can be normalised to unimodal distributions leading to better estimators (see figure).

Discussion
Unfolding may be necessary to reveal and enhance periodicity in electrophysiological time series and is therefore proposed as a pre-processing step before analysing HRV, independently from the method used for recording and analysis of the heart beat sequences.

The reduction of HRV after seizures demonstrates that epilepsy patients are not only at risk during the seizure but in addition suffer from lasting alterations of the autonomous nervous system, which may put their lives at risk.



Influence of Mobile-Bearing Position on Bone Strain and Primary Stability after Total Ankle Replacement: an in vitro study

Jonas Guerdat

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Introduction

Total Ankle Replacement (TAR) offers the advantage of preserving ankle joint motion compared with ankle arthrodesis. However, compared to hip or knee arthroplasty, TAR is a less successful procedure when considering the relatively low implants survival rate at 10 years, the high revision rate and also numerous complications. The main complications after TAR are periprosthetic cysts (up to 77% of cases), fractures of the malleolus and bone loosening [1] [2]. However, the mechanism that leads to these complications remains unclear and the high incidence of periprosthetic cysts raises worries for long-term survivorship of the implants. Therefore, there is a need for better understanding of shortcomings associated with TAR, and for improvement in implant design and surgical technique.

Goal

To determine, in vitro, the influence of mobile-bearing position on bone strain and primary stability after Total Ankle Replacement by measuring bone surface strain and bone-implant relative movement. The study was focused on tibial components.

Materials and Methods

Prostheses from the company Tornier were implanted in 8 cadaveric tibiae by an experienced surgeon. A load of 2000 [N] was applied on the prosthesis at three different positions: posterior, neutral and anterior. The displacement was measured on the anterior surface of the tibia using 3D Digital Image Correlation. The bone axial strain was then evaluated from the displacement.

Fig. 1 The Salto – mobile version prosthesis. X-ray front view (source: Dr. Xavier Crevoisier)

Results

Bone strain was higher when the mobile-bearing was placed in the anterior position compared with the neutral position ($p < 0.00001$) and smaller when placed in the posterior position ($p < 0.00001$). The order of magnitude of bone strain varied from +500 [με] up to -5600 [με]. Most of the time, the maximum compressive strain was found around the keel of the implant. The bone-implant relative movements showed a mean value (± SD) of 142 ± 40 [μm] for the neutral position.

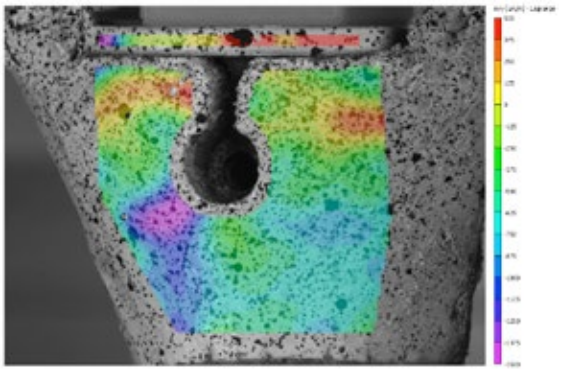

Fig. 2 Bone axial surface strain on the anterior part of the tibia. Maximum strain in purple

Discussion

The axial strain measured on the anterior bone surface was for most of the tibiae in the physiological zone, between 200 and 2000 [με] according to Frost (1987). However, some values mainly measured around the keel of the implant reached the pathological zone where the risk for bone fracture is higher (> 4000 [με]). The bone-implant relative movements were in the same order of magnitude of in vivo measurements reported in the literature. In conclusion, we confirmed the importance of mobile-bearing position in TAR, which could be optimized during surgery.

References

[1] Crevoisier et al. (2006) – Les prosthèses de cheville: un défi prometteur
[2] Rodriguez et al. (2010) – Medium term follow-up of the AES ankle prosthesis

Acknowledgements

The prostheses and the tools for the surgery were provided by Tornier. We are grateful to Mr. Ratron who was the person of contact. We would like to express our gratitude to Dr. Xavier Crevoisier who performed all surgical procedures for this project.

Effects of Hypoxia on Three Dimensional Mesenchymal Stem Cell Microcarriers for Intervertebral Disc Repair

Stephan Häfner

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Examiners: Prof. Dr. Benjamin Gantenbein and Dr. Jivko Stoyanov

Background

A new developing treatment for degenerated intervertebral discs (IVD) is cell-mediated tissue regeneration. In this regard a promising approach is the *in vitro* culture of mesenchymal stem cells (MSCs) on three dimensional microcarriers. Cell-microcarrier can be minimally-invasive transplanted into IVDs by injection. This study was designed to develop a suitable microcarrier model to culture MSCs under different oxygenation levels in static and dynamic conditions, aimed to optimize matrix synthesis towards IVD-specific proteins.

Project Scope

Human bone marrow MSCs were cultured on equine collagen microcarriers, derived from medically approved devices. 40'000 MSCs were seeded per 5 mg of microcarriers (dry weight), expanded for 7 days, and differentiated to chondrogenic lineage for 21 days. 2%, 5% and 10% hypoxic cultures conditions were compared to normoxia (21%), in static and dynamic cultures. Cell number was measured by Presto Blue™ cell viability test. Evaluation of matrix synthesis pattern was conducted by qRT-PCR and total GAG and DNA quantification at the end of cultures. Immunohistochemical analysis qualitatively visualized matrix deposition in the differentiated cell constructs.

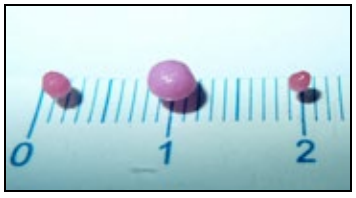

Figure 1. *MSC tissue constructs at day 28 in static culture in normoxia (**A**) and 5% hypoxia (**B**), and in dynamic culture in 5% hypoxia (**C**) culture conditions. Identical starting conditions of 40'000 MSCs and 5 mg BIOPAD Collagen microcarriers. (Scale unit = 1 cm)*

Results

Differentiated cell constructs at day 28 appeared in single, tough rubber-like ball structures of different shapes depending on the type of culture (Fig. 1). 5% hypoxia and dynamic cultures significantly increased cell proliferation rate of two-fold, compared to normoxia and static cultures. During differentiation, the highest cell number, gene and protein expression of disc extracellular matrix molecules, namely proteoglycans, collagen type II and aggrecan, was obtained in static conditions and 5% hypoxia (Fig. 2).

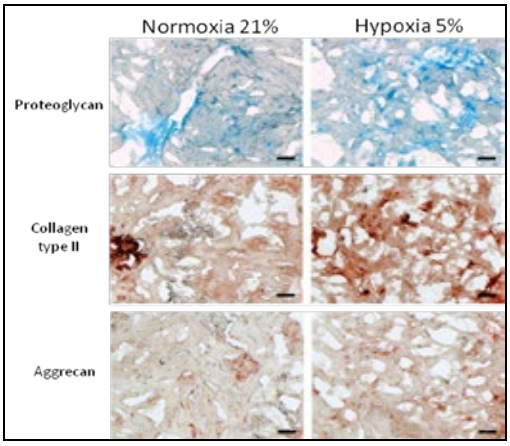

Figure 2. *Histological and immunohistochemical stainings of cell constructs at day 28, cultured in either 21% or 5% O_2 in static conditions. Proteoglycans are stained in blue by Alcian Blue (upper row), and collagen type II and aggrecan are depicted in red respectively (lower rows). (Scale bar 100 µm)*

Discussion

These results demonstrated that microcarriers made of equine collagen are a suitable support for differentiation of MSCs to disc-like cells. Hypoxia clearly demonstrated advantages in MSC culture for proliferation and differentiation enhancing extracellular matrix synthesis. The used dynamic culture setting was appropriated for cell proliferation but not differentiation.

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Bearings for Intracorporeal Energy Harvesting Devices

Ben Hausammann

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Introduction

Many implantable devices such as pacemakers, defibrillators or neurostimulators require electrical power supply, which is usually realized by internal primary batteries which have to be replaced after a certain time period. In order to improve patient's quality of life and to prevent repeated device replacement procedures, it is highly desired to develop devices that are able to harvest intracorporeal energy. An on-going project aims at extracting 1 mW of hydrodynamic power from a non-vital artery by the use of a miniature turbine device.

The aim of the present master's thesis was to assess and develop suited bearings for the microturbine. Bearings are one of the most crucial components in mechanical energy converting devices. Their task is to guide rotational and/or linear motion between two relative moving parts and support intrinsic and extrinsic forces produced by the device or the environment. The challenge is to design the bearing system in a way to provide least friction in order to increase machine efficiency and lifetime.

Materials and Methods

Rotational speed of the turbine rotor as well as support forces had been evaluated. Environmental influences like position or movements of the human body and blood properties had been investigated and composed to a requirement specifications list.

An extensive literature research with special scope in the MEMS (Micro-Electro-Mechanical Systems) and watch industry in combination with rough dimensioning and friction torque calculations was performed.

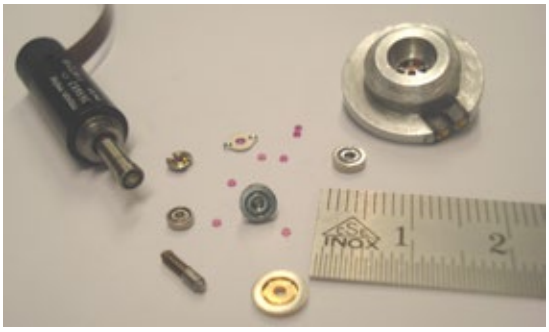

Fig. 1 Micro DC-motor, selection of miniature-bearings and micro machined parts used for bearing characterization

A selection of conventional micro bearings (Fig. 1) was chosen in order to prove calculated friction losses.

Further, a multipurpose test rig (Fig. 2) has been developed and built to characterize torques consumed by microbearings or produced by tiny electrical generators as present in the miniature turbine.

Results

It was found that preferred contactless support systems such as hydrodynamic or diamagnetic bearings are not sufficiently suited in terms of design size and/or reliability and therefore security.

The final result of review and tests is the proposal to apply microball bearings to gain benefits of a low friction, stable, and durable and bearing system independent of physiological effects.

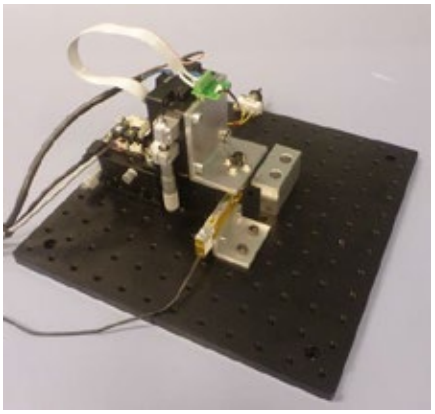

Fig. 2 Picture of the multipurpose bearing test rig assembly

Discussion

It was possible to obtain reliable results for the micro generator. Complexity of force induction in two perpendicular directions, speeds from 500-5000 rpm while monitoring forces in the in the mN range and torques in the sub µNm range lead to basic constructional inconsistencies making it impossible to measure the low bearing torques expected form the analytic predictions.

Differential measurements of the developed bearings mounted on the turbine prototype with the purpose of comparing wear, durability and friction simultaneously is suggested.

Effects of Implant Surface Topographies on the Peri-Implant Micro-Environment

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Examiners: Prof. Dr. phil. nat. Willy Hofstetter and Dr. Reto Luginbühl

Introduction

Materials implanted into human tissues evoke a host *vs*. graft response. During the process of healing, the tissue - implant interactions will be influenced by the surface characteristics (i.e. composition, chemistry, and topography) of the implant. Moreover, the release of growth factors and cytokines by cells getting into contact with an implant will modulate the cellular activities in the peri-implant tissues (Anderson et al., 2008). Previous results have demonstrated that the topography of the surface plays a decisive role in the activation of cells from the monocytic lineage (Brunette DM, 1996). The cells' reaction to the implant is considered a determining factor for the composition of the peri-implant micro-environment. Successful osseointegration of orthopaedic or dental implants depends mainly on the activity of osteoblasts and osteoclasts which form and remodel the bone at the implant-tissue interface. The relationship between monocyte derived macrophages and cells belonging to the osteoblast lineage is not fully understood. Therefore, we investigated the effects of surface topographies of Titanium (Ti) disks on macrophage adhesion, proliferation and cytokine secretion and on the modulation of osteoblast lineage cells in co-cultures.

Materials and Methods

Analysis of surface topographies and of cells on Ti disks was performed by scanning electron microscopy (SEM), Hoechst and actin stainings were analyzed by fluorescence. Cell proliferation was evaluated by DNA measurements and the number of viable cells was assessed using a XTT kit. Osteoblast differentiation was characterized by alkaline phosphatase (ALP), osteoclast development was followed by analyzing the synthesis of tartrate-resistant acid phosphatase (TRAP) expression. Levels of colony-stimulating factor 1 and 2 (CSF1, CSF2), tumor necrosis factor-alpha (TNFα), Interleukin 1-beta (IL-1β), interleukin 6 (IL-6), and osteoprotegerin (OPG) were analyzed by enzyme linked immunosorbent assay (ELISA).

Results

The release of interleukin 6 (IL-6) and osteoprotegerin (OPG) from co-cultures of *wt* osteoblasts and RAW 264.7 cells seeded on machined (Ma), water blasted (Bl), acid-etched (AE), and acid-etched + water blasted (SLA) was determined. IL-6 levels were significantly up-regulated ($p<0.05$) in cultures, in which the RAW 264.7 cells were grown on acid-etched surfaces as compared to other surfaces. The use of anti-TNFα antibodies resulted in a significant decrease of osteoblastic IL-6 production and a concomitant up-regulation of OPG. The dependence of the release of IL-6 on TNFα was confirmed in co-cultures of RAW 264.7 cells with osteoblast lineage cells from $p55TNFR^{-/-}/p75TNFR^{-/-}$ animals.

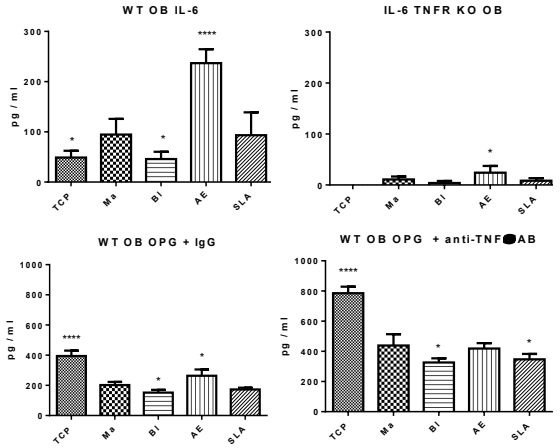

*Fig. 2 interleukin 6 (IL-6) and osteoprotegerin (OPG) released in co-cultures of RAW cells and osteoblasts after 72 hours. IL-6 release was compared in co-cultures using wt osteoblasts and $p55TNFR^{-/-}/p75TNFR^{-/-}$ osteoblasts. Osteoprotegerin (OPG) production in co-cultures with IgG (control) was compared to co-cultures supplemented with anti-TNFα antibody. Statistically analysed by one-way ANOVA and Tukey post-hoc test. Tissue culture plate (TCP), machined (Ma), water blasted (Bl), acid-etched (AE), and acid-etched + water blasted (SLA). *p<0.05 Compared to machined (Ma). (n=5 to 6).*

Discussion

In the present study, we found RAW 264.7 cells to induce osteoblastic IL-6 release in dependence of the surface topography of Ti disks they were grown on. The data suggests that the composition of the micro-environment around an implant *in situ* can be affected by the surface topography of the implant. Moreover, the production of cytokines by monocyte/ macrophage lineage cells can affect the development of bone cells in the peri-implant site and as may modulate the kinetics of bone healing. IL-6 may stimulate osteoclast development and activation and as a consequence may increase bone turnover leading, to a local high bone turnover and an acceleration of osseointegration.

References

Haynes et al., Regulation of bone cells by particle-activated mononuclear phagocytes, Bone Joint Surg Br November (1997) vol. 79-B no. 6 988-994

A Collagen Derived Matrix (CDM) for Treatment of Articular Cartilage Lesions

Deborah Herz

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Introduction

Hyaline articular cartilage covers and protects bone ends in joints. Collagen is a main component and chondrocytes, with 1% of tissue volume represent the only cell type within this tissue. Cartilage has a limited self-repair capacity and therefore cell-based therapies like ACI (Autologous Chondrocyte Implantation), MACI (Matrix-assisted Autologous Chondrocyte Implantation) and AMIC (Autologous Matrix Induced Chondrogenesis) are the current treatments of choice. In these treatments collagen scaffolds are applied to keep injected, seeded or absorbed cells in place, and to assist in cartilage matrix formation. However, clinical results remain unsatisfactory. To improve cartilage regeneration, a new collagen derived sponge (CDM) was developed. The sponge is designed to fill the entire volume of the lesion thereby maintaining the cartilage volume, and to favor the induction of neochondrogenesis.

Goal

The main goal of this project was to demonstrate that the CDM sponges support neochondrogenesis *in vitro*. To this end chondrocytes have been chosen as a cell type due to their established and consistent chondrogenic potential.

Materials and Methods

Primary articular chondrocytes from a total of 6 donors were expanded in monolayer culture in DMEM/F12/10%FCS. Chondrogenesis was induced in DMEM/F12/10%FCS, in a chondrogenic serum-free medium in the absence/presence of TGFβ1 and dexamethasone, absence/presence of hyaluronic acid (HA) and under normoxia (21%O_2) and hypoxia (5%O_2). Cell viability was analyzed via Live/Dead stain under fluorescent microscope. The analysis of pellets and sponges comprised macroscopic evaluation, histology (proteoglycan and collagen deposition), immunohistochemistry (synthesis of collagen type II) and biochemistry (GAG/DNA).

Results

The sponge structure was analyzed macro- and microscopically. CDM architecture displayed two different types of pores: honeycomb like pores at the periphery and columnar pores in the centre (Figure 1 A). The cytotoxicity and endotoxicity tests indicated that the sponges are biocompatible. Optimal cell seeding conditions, including statical versus orbital seeding, cell numbers and proliferation time in sponges were determined and demonstrated cell attachment and even distribution within sponges. Chondrocyte viability evaluation confirmed the presence of living cells in sponges upon 1 and 4 days of culturing. Optimal chondrogenic conditions comprising hypoxia 5%O_2, hyaluronic acid, and TGFβ1 and dexamethasone were defined in pellet culture and applied for neochondrogenesis in sponges. Upon chondrogenic incubation for three weeks, chondrogenesis was confirmed in pellets. In sponges cells were evenly distributed within CDM and produced sulfated proteoglycan and collagen type II mainly on the surfaces (Figure 1 B).

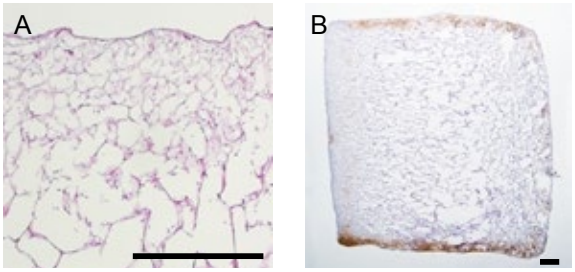

Figure 1: Histological pictures of CDM sponge. (A) H&E stained sponge showing pore structure. (B) Collagen II production made visible by IHC. Bar: 500µm

Discussion

This study demonstrates preliminary investigation of CDM sponges *in vitro*. The obtained results indicate that CDM represent a biocompatible scaffold which supports neochondrogenesis of human articular chondrocytes in vitro. Deposition of collagen type II mainly on the surface of the sponges could indicate that pore geometry might be a key to scaffold assisted successful cartilage tissue regeneration as previously suggested [1].

The CDM sponges are still in their testing phase and are not commercially available.

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Acknowledgements

The project was supported by Geistlich Pharma AG.

Development of a novel Anterior Cruciate Ligament (ACL) reconstruction technique

Ramon Hüppi

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Examiners: PD. Dr. Philippe Büchler and Nicolas Bouduban

Introduction

Nowadays, interference screws with bone tendon bone (BTB) grafts is the gold standard surgical procedure for the reconstruction of the anterior cruciate ligament (ACL). Despite a wide range of established solutions, several clinical problems remain. Present soft tissue fixation device within an intratunnel or an extratunnel fixation may not possess the same biomechanical or biological properties as a BTB graft. Another issue is that they do not seal enough and synovial fluid could flow into the bone tunnel. This could lead to a bone tunnel widening. The objective of this thesis was to propose a novel fixation device for a soft tissue graft which should maximize the implant anchorage, provide a good sealing of the reconstruction and limiting the risk of damaging the graft material.

Materials and Methods

Initially, five implant concepts were proposed for the femoral fixation. A detailed benefit analysis was performed and three concepts were selected. After a dry lab, two of them were further optimized with the use of inputs like feasibility of injection moulding, FE analysis and mechanical testing. The best implant was determined based on mechanical testing. The final implant design was submitted to leading surgeon during a cadaver lab in order to assess and optimize its surgical usability.

Results

Two implants were developed; one for the femoral fixation and sealing and one for the tibial sealing. With a flow analysis the productibility of the femoral fixation implant was verified.

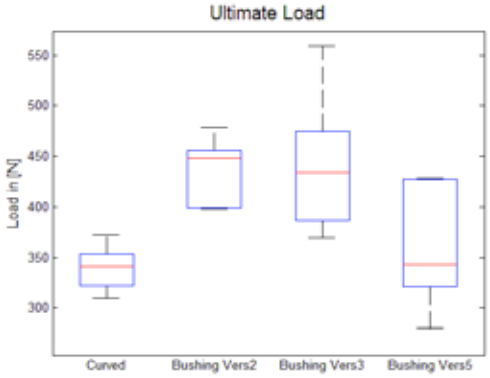

Fig. 1 Ultimate pull-out load of the different implant designs in a synthetic bone block

Mechanically the best implant could be found, which is well anchored in the cortex of the femur, seals well and conserves the graft. The FE simulation has shown that the implant should withstand an applied pull-out force of minimum 600N without any critical deformation of the implant. The structural properties and load-to-failure of the femoral fixation were mechanically tested. Results indicated the superiority of one of the proposed design over the other concepts. In this case, the ultimate load was 847±176N in a cadaveric bovine bone.

Discussion

An implant corresponding to the mechanical and sealing requirements was successfully proposed. The mechanical tests and the cadaver lab have shown that this implant is able to support loads corresponding to in-vivo situation. In the cadaver lab an appropriate surgical technique for this type of implant was defined. The lab had also confirmed that the graft could be grabbed with the extended implant wing. The reached ultimate pull-out load behaviour of the femoral fixation device could not be properly validated with concurrence product, because the mechanical tests with the interference screw failed. In the literature [1] there could be found a mean pull-out load of 507±97N which was reached with an ∅8x23mm bioabsorbable interference screw tested in a cadaveric bovine tibia. The cadaver lab indicated that the interface between the placement instrument and the implant has to be more rigid. Also a better solution to secure the implant in the bone is required to replace the metallic screw which is currently used. Additional work is also required for the validation of the tibial sealing device.

References

[1] A. Weiler, R. Hoffmann, A. Stähli, H. Bail, C. Siepe und N. Südkamp, «Hamstring Tendon Fixation using Interference Screws: a Biomechanical Study in Calf Tibial Bone,» *Arthroscopy,* Bd. 14, pp. 29-37, 1998.

Acknowledgements

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Augmented Reality X-ray II

Kaspar Jäggy

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Examiners: Prof. Dr. Philippe C. Cattin and Dr. Hans W. Roser

Introduction

Creating a planar X-ray image of good quality is a challenging task for medical doctors or radiographers (MTRAs). All parameters on the X-ray device have to be set correctly but sometimes even more difficult is the adequate placement of the patient. Often a bone or joint has to be imaged from a very specific angle to have the best view of the object.
An education and training device for MTRAs able to simulate a planar X-ray image with given parameters and pose of the patient is highly demanded by radiologists responsible for education.

Materials and Methods

This thesis covers the development of a first prototype able to simulate planar X-ray images of the head reconstructed from a 3D CT-dataset. An already existing ray casting algorithm, with which digitally reconstructed radiographs (DRR) can be produced, is adjusted to meet the geometrical properties of the gantry used for this project. By searching the nose tip and its orientation in a depth image acquired by a Kinect, the pose of the patient's head is detected.

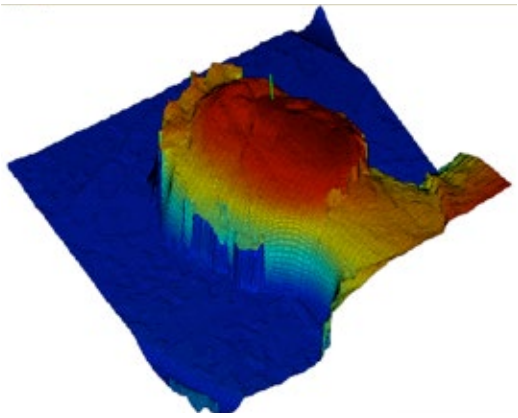

Fig. 1 3D reconstruction of a head with its detected orientation depicted by a green arrow.

Both, the pose of the head and the rotation of the gantry are taken into account to calculate the DRRs. Finally, the contrast of the DRRs is adjusted by histogram Specification to match the appearance of real X-ray images.

Results

In the graphical user interface (GUI) a DRR can be calculated incorporating all geometrical properties of the X-ray apparatus. Although some parameters and conditions such as the illumination or the energy spectrum produced by the source are not emulated the resulting DRRs look similar to real X-ray images.

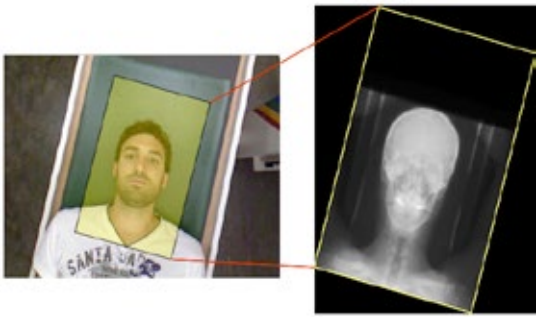

Fig. 2 The field-of-view overlaid on the color image with its respective DRR.

The method developed in this thesis to estimate the pose of the patient's head is very robust. In all test images the correct nose tip is found. In particular for frontal and nearly frontal head images, the orientation of the head can be estimated accurately. The accuracy of the head pose estimation in side view images decreases due to missing depth information of parts of the nose which are not seen by the Kinect.

Discussion

A promising first prototype of an X-ray simulation application has been developed. The geometrical properties of the X-ray apparatus could be emulated correctly. The algorithm presented for estimating the pose of a head from depth images captured by a Kinect works as intended. Although the application shows good results, ongoing research and development is needed to develop a device which can be used for education purposes.

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E²corder (Esophageal ECG Recorder): Low-Power Analog Hardware Design

Silvan Kojic

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ARTORG Cardiovascular Engineering, University of Bern
Examiners: Prof. Dr. Josef Götte and Prof. Dr. Rolf Vogel

Introduction

Heart rhythm disorders (arrhythmias) can be associated with fatal outcomes such as sudden cardiac death or cerebral apoplexy. The surface electrocardiogram (ECG) using skin electrodes attached to the chest wall and the limbs is the clinical gold-standard to detect the presence and to characterize the type of arrhythmia. However, many patients suffer only from short-lasting, rarely occurring episodes, and therefore require long-term ECG recordings in order to establish the diagnosis and define the therapy. The probability to detect such paroxysmal arrhythmias increases with the recording duration. Regrettably, surface ECGs suffer from two important limitations. First is the limited sensitivity for the electrical activity of the atria, which is crucial for modern treatment strategies. Second is the limited suitability for clinical long-term studies, which is related to electro-mechanical contact problems of the skin electrodes and their potential to harm the skin. As a promising alternative, ECG signals are captured from the esophageal mucosa. These signals offer detailed information on atrial activity, and the esophagus allows long-term instrumentation with excellent electromechanical contact.

Fig. 1 Esophageal ECG recording by a catheter

Methods

The goal of this thesis has been to research and to design ultra low-power front-ends which interfere as little as possible with the sub-millivolt input signals. The signals must be conditioned in a manner that they are ready for further processing. Off-the-shelf components solutions (discrete circuits) and integrated circuits were designed and simulated. The discrete circuits were built on a PCB and measured.

Results and Discussion

In comparison with the existing first prototype, the new discrete version consumes less then 10% power, which corresponds to a current of 12µA at a supply voltage of 1.8V. Measurements on the discrete evaluation board lead to the conclusion that the used circuit fulfills all requirements concerning frequency and phase response, sufficient low noise characteristic and a high common mode rejection ratio.

Fig. 2 Discrete Evaluation Board

In order to further reduce power consumption and especially to reduce area needs, an integrated implementation has been designed, which can be realized in an ASIC (Application Specific Integrated Circuit). Using the Nagaraj technique in the simulation of switched capacitor circuits, the challenges of large time constants (more than one second) and the associated large capacitor areas can be overcome. Large time constants are given by the low-frequency spectral characteristic of ECG signals. Frequency and phase response proved that this applied approach is well-suited. Supply currents in the sub micro-ampere are attainable.

Acknowledgements

This project is supported by grant no 10717.1 of the Swiss Commission of Technology and Innovation (CTI).

Development of a Wireless, Two Channel Transcutaneous Electrical Stimulator for Tactile Sensation

Daniel Lachner Piza

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Examiners: Prof. Dr. Volker M. Koch and Prof. Dr. Kenneth James Hunt

Background

The sense of touch constitutes a vital feedback for a person during interaction with the environment. The sense-actuate closed loop can be broken in the case of certain pathologies or amputation. With the aim of reestablishing or relocating sensory feedback, this project deals with the development of two portable, dual-channel, wireless, synchronized, transcutaneous electrical stimulators with output current monitoring. The generated signal is intended to stimulate the tactile sensory receptors located on the lower back.

Project Scope

To study the body's response to stimulation given different stimulation parameters, the stimulator shown in Figure 1 is controlled by a PC via Bluetooth. A GUI has been developed to modify stimulation parameters, switch modes, display output voltage, current and skin resistance.

Figure 1

The stimulation signal as shown in Figure 2 is square and biphasic, aiming to deliver a charge-balanced stimulus. The carrier frequency ($1/[t_1+t_2]$) can be set to a value from 1 kHz to 10 kHz, the envelope frequency ($1/T_P$) from 1 Hz to 200 Hz. It is also possible to stimulate continuously with the carrier frequency ($T_P=t_b$). The stimulation amplitude can be chosen from 2.3 V to 30 V.

The output current monitoring feature allows generating similar sensations across the electrodes, independent of changes in the body impedance.

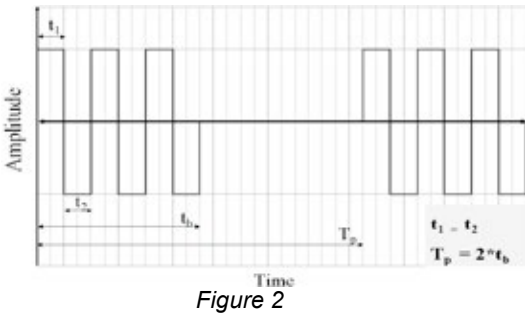

Figure 2

As shown in Figure 3, a moving sensation can be produced, which is a tactile illusion generated by the synchronized stimulation of tactile receptors by two channels with accordingly rising and falling amplitudes. The stimulus is perceived as a one dimensional movement between the two electrode pairs, which can be used as a form of sensory feedback.

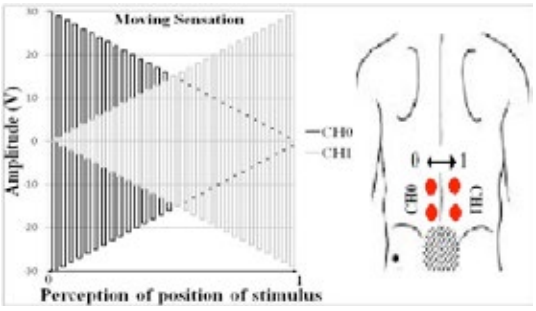

Figure 3

Results and Discussion

The stimulator successfully generates the desired signals and the GUI allows a smooth interaction. Currents are monitored on every positive phase and displayed on the PC where the electrode-skin interface resistance is calculated. Further tests on humans are yet to be performed in order to characterize the body response to the different stimulus parameters.

Mechanical Properties of the Human Intervertebral Disc

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Introduction

Prediction of bone strength using finite elements (FE) simulation based on CT images shows great promise. However, in FE modelling boundary conditions have an impact on the fracture risk predictions. Thus, realistic loading conditions should be used. The most recent FE models load the vertebra via an idealized intervertebral disc (IVD) but, a patient-specific and degeneration sensitive model of the IVD is the next step in the human spine modelling. Therefore, the aims of this project are to assess the impact of IVD degeneration on its mechanical properties and to develop tools to compare these experimental results to FE predictions.

Materials and Methods

14 function spine units (FSU) were cut out of 6 human lumbar spines. Facet joints and soft tissue but IVD were removed and the FSU's vertebrae were embedded in PMMA. MRI images of the specimens were performed to produce FE models of the IVDs and assess their degeneration grade using Pfirrmann's scale [1]. Flexion/extension, lateral bending and axial rotation were tested by applying a pure moment of 5Nm to the upper vertebra. Resulting intersegment motions were measured using an optoelectronic motion capture system.

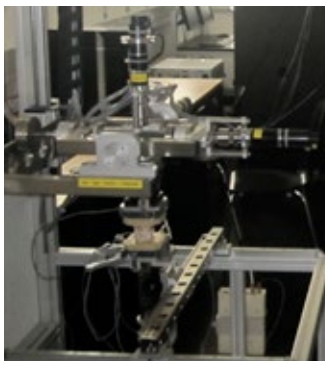

Fig. 1: FSU mounted on the Spine Tester.

Experimental data were then processed by custom made Python scripts and the range of motion (RoM) [°] and the stiffness [Nm/°] were analyzed. A MRI-based FE model of a healthy specimen was generated and the same load-cases were simulated using two different constitutive laws for the IVD (hyper-elastic isotropic & anisotropic). Experimental and simulation data were then compared using another custom made Python script.

Results & Discussion

Out of 14 FSU, 2 were considered to be of grade I degeneration, 6 grade II, 7 grade III and 2 grade IV. If doubt, the IVD was attributed to both grades. General behaviours during the mechanical tests (MT) were in agreement with the literature [2][3]. The RoM tended to increase and the stiffness to decrease with the level of degeneration. These results could be explained by the biochemical and micro-structural changes that occur in the IVD during degenerative process. Moreover, comparisons between FE predictions and experiments showed good agreement for all load-cases but axial rotation. This suggests that the constitutive law requires further improvement. Nevertheless, the constitutive law modelling collagen fibres (anisotropic) fitted experiments better than the isotropic one. Finally, the quality of the scripts could be assessed using statistical tools [4]. A maximum error of only 1.5% was computed for the overall process.

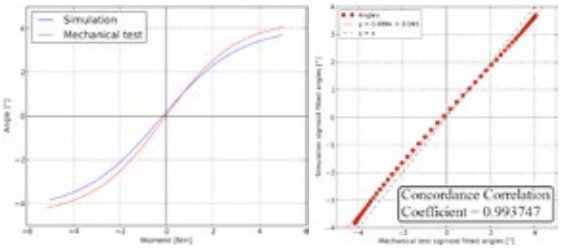

Fig. 2: FE/experiment comparisons. Quantitative comparisons of Moment-Angle curves (left). Qualitative correlation FE/experiment (right).

Conclusion & Outlook

The results of the experiments were consistent but further study would require more tests with a higher number of FSU. The scripts are reliable and provide automatic and precise comparisons between FE predictions and experimental results. Anisotropy improves the FE predictions but refinement of the constitutive law is needed (cf. axial rotation).

References

[1] Pfirrmann & al. 2001.
[2] Tanaka & al. 2001.
[3] Haughton & al. 1999.
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Acknowledgements

Thanks to the ISTB and its entire staff for the help and the support provide during the whole project.

Development of a Steerable Catheter Concept for Percutaneous Heart Procedures

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Introduction

The morbidity and mortality associated with conventional surgical “open heart” procedures are not negligible and less invasive techniques providing a percutaneous, minimally invasive approach are more and more gaining importance.
The aim of this thesis was to develop a concept for a scalable steerable catheter to gain access to specific target areas inside the heart to complete a variety of minimally invasive procedures.
For a first prototype and for creating a specific design input, one particular application was targeted, namely a trans-septal approach to the right atrium via the femoral vein.

Materials and Methods

A standard product development process according VDI 2222/ ISO 13485 was applied, going through analysis, concept, drafting, detailing, prototyping and test phases. The development of the steerable catheter was segmented into three subassemblies, namely handle arrangement incl. actuators, catheter shaft and steerable distal section. The catheter must furthermore fulfill the requirements according ISO 10555-1.

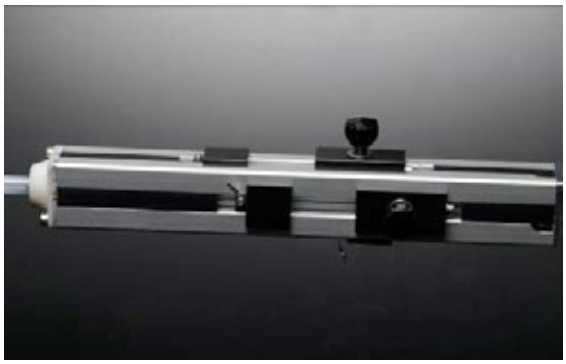

Fig.1: Evaluation model of a linear handle with an integrated force amplification system

Outcome tests included distal end range of motion verification, actuation force measurements and endurance tests of the distal end.

Results

Two adequate handle variants with stainless steel cables as force transmitting elements were developed. A steerable distal end with the required range of motion and strength was engineered during the thesis project. In addition a catheter shaft with adequate torsional and bending stiffness was elaborated using an extruded multi-lumen profile in combination with braided tube.

*Fig. 2: Range of Motion study (multiple exposure photography) of a l*aser-cut distal end with the ability of 3-way bending.

Discussion

The final tests confirmed that both developed handle variants are capable of generating the required forces in an ergonomic manner.
The distal end showed very smooth and accurate motion properties and sufficient strength, but still requires further testing.
In general, the concluding design verification was successful as the acceptance criteria previously set in the design input were met.

Thermo-Reversible Hydrogel for Nucleus Pulposus Replacement: Feasibility under Static Loading in a mild Papain-Induced Disc Degeneration Model

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Background

Nucleus pulposus (NP) replacement by the application of injectable hydrogels seems a straightforward approach for tissue engineering. We investigate a thermo-reversible hydrogel (TR-HG), based on a modified polysaccharide with a thermo-reversible polyamide (poly(N-isopropylacrylamide = pNIPAAM). Using “click chemistry” and reversible addition fragmentation transfer (RAFT) polymerization the gel is made to behave as a liquid at room temperature and hardens at >32°C. In order to inject the hydrogel, a mild papain disc-degeneration model (PDDM) is employed that creates a cavity in the intervertebral disc (IVD). Here we investigate the performance of the TR-HG with or without preconditioned human mesenchymal stem cells (hMSC) with rhGDF-5 *in situ* in bovine IVD under static loading for 7 days.

Project Scope

IVDs from fresh calf-tails were harvested including cartilage endplates. The experimental design included i) PBS injection (untreated control) ii) PDDM + PBS injection (PDDM control) iii) PDDM + TR-HG + bovine NPCs (Cell control) v) PDDM + TR-HG + hMSC. Autologous NPC and Primary hMSCs were seeded at 4M cells/mL in 3-D in the TR-HG for 7 days prior to disc injection. Reversal of gel into fluid allowed injection of gel+cell mixture into NP cavity created by PDD. All discs were subsequently placed under static loading of 0.1MPa for 7 days using custom designed specimen chambers.

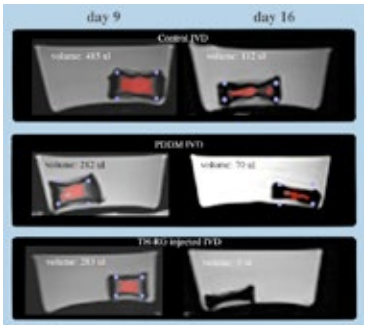

Figure 1. MRI segmentation of Control disc, PDDM disc and gel+cell injected discs before and after 7-day static loading.

Magnetic Resonance Imaging (MRI) was employed to image the hydrogel-filled cavity before and after loading (Fig. 1). While cell samples were collected at 3 different time points for cell viability and gene expression analysis. Final sulphated glycosaminoglycan synthesis and DNA content were also performed from annulus fibrosus (AF) segments of each disc.

Results

MRI images confirmed a central positioning of the TR-HG into the PDDM. A considerable drop in volume across all groups in the NP region and consequently of disc height was observed. Gene analysis of injected hMSCs showed significant differences between day 8 and day 16 for Acan, Col2a1, Vcan and Sox9 relative to day 1 (Fig. 2). Cell viability of injected cells dropped from around ~100% down to ~70-80% for bovine and hMSCs throughout the study. GAG/DNA ratio in the untreated discs was significantly retained compared to all other PDD-induced treatment groups.

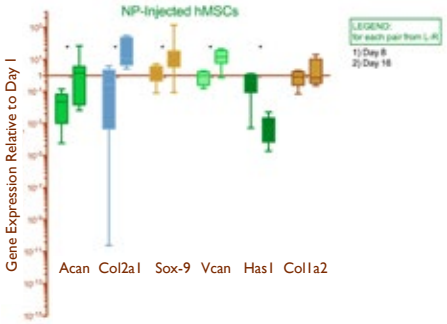

Figure 2. Gene Expression of injected hMSCs relative to day 1 showing significant differences.

Conclusion

MRI imaging of TR-HG seems a promising protocol for non-invasively observing gel performance in situ. Although 10% TR-HG does not seem to be able to bare any mechanical loading, it is a nonetheless a feasible scaffold for in vitro 3D preconditioning of hMSCs with minimal loss of cell viability. Furthermore the cells are able to survive and differentiate into chondrocyte-like cells after injection into whole organ IVD culture of 7 days under static loading.

Development of an Intra-Vaginal Sensor for Measuring Pelvic Floor Muscle Activity

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Introduction

Numerous women suffer from pelvic floor disorder, which can generate, amongst others, stress urinary incontinence (SUI) [1]. SUI is a particularly prevalent type of incontinence that is defined as the "complaint of involuntary urine leakage on effort or exertion, or on sneezing or coughing" [1]. Several theories have attempted to explain female urinary continence mechanisms emphasizing the importance of the pelvic floor muscles (PFM) in urethral closure for maintaining continence [1]. Nevertheless, several studies [2] mentioned the lack of suitable instrumentation to assess PFM activity. Therefore, we aimed to ameliorate this significant diagnostic problem that prevents physiotherapists and medical doctors from understanding the pathophysiology of SUI.

Materials and Methods

In order to provide a better understanding of the mechanisms of PFM contraction and its influence on SUI, two chemically disinfectable intra-vaginal sensors were developed. They allow to measure pelvic floor muscle activity and strength as well as movement characteristics; in particular: a) the static and dynamic PFM strength in the transverse plane, 2) the rate of force development, 3) the electromyogram, and 4) three-dimensional position and orientation changes of the probe during a PFM contraction. The intra-vaginal sensor prototype I (Fig. 1) is composed of four measurement platforms enabling force and electromyogram measurements in two directions (anterior/posterior and lateral/lateral), while the intra-vaginal sensor prototype II (Fig. 2) is a lightweight version composed of only two measurement platforms. Each measurement platform is equipped with a pair of electrodes and a force sensor based on thin film strain gauge technology connected to an external amplifier. Orientation and position of both sensors within the vagina is tracked by a six degrees-of-freedom electromagnetic tracking device (trakSTAR, Ascension Technology Corporation).

Fig. 1: Intra-vaginal sensor prototype I (Image source: arteplus.ch)

Results

Non-linearity test results of each force measurement platform showed an absolute full scale measurement error of less than 2 % over the whole platform in the range from 0 N...10 N. Preclinical tests on a few healthy subjects showed that the developed probes are complementary: while the intra-vaginal sensor prototype I, in some cases, might prevent practitioners from studying functional contractions during physical activities (walking, climbing stairs, etc.), the intra-vaginal sensor prototype II provides less functionality but a better stability due to its reduced weight and improved design.

Fig. 2: Intra-vaginal sensor prototype II (Image source: arteplus.ch)

Discussion

The results suggest that these investigational devices fully meet the defined user and system requirements and are ready for human use. Approvals from the competent Ethics Committee and Swissmedic are pending.

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UNIVERSITÄT BERN

Augmented Reality X-Ray

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Introduction

The use of X-rays has always been common in medical imaging fields, such as diagnostic radiography, in order to reveal the internal structures of the body. Planar X-rays remain a standard cornerstone technique to visualize a large number of anatomical structures. However, capturing planar X-rays is not trivial, since different settings such as the exposure and the field-of-view must be optimal. Moreover, the relative positioning of the target anatomical structure to the X-ray device is difficult, and therefore considered as a key point, in order to get the best view of a specific bone. In addition, X-rays are ionizing radiations, hence, the dosage to the patient must be kept at a minimum level. Thus, additional X-rays due to bad settings or pose must be avoided. The following project aims to develop a system capable of simulating planar X-rays based on the settings of typical input parameters of an X-ray machine and the pose / position of the hip bone. The goal of this simulator is to mimic as close as possible real X-rays, to help radiologists to find the optimal settings of the machine and optimal pose of the target anatomy, prior to taking real X-rays.

Materials and Methods

Using the Kinect 3D camera sensor by Microsoft Xbox 360 gaming console, a calibration procedure is performed, in order to get accurate spatial depth information from the raw data delivered by the Kinect. After calibration, the 3D scene observed by the camera is well-defined in meters. In a second step, image processing methods are used on the calibrated depth maps and color images to define the exact pose of the anatomical structure (position and orientation) relative to the X-ray apparatus. Once the hip bone is spatially fully located, a DRR (Digitally Reconstructed Radiograph) technique simulates an X-ray from a CT model, using the hip pose estimation results and the control settings the user can define in the Graphical User Interface

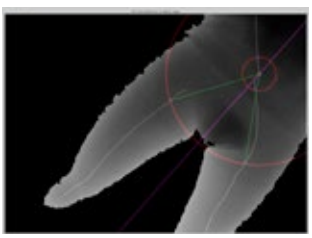

Fig.1: Hip bone detection and pose estimation from Kinect depth maps

Results

Visual evaluation shows that the DRRs obtained mimic well the X-rays of the hip bone region according to its pose. The DRRs' contrast is satisfactory and the hip bone appears clearly. The DRRs depict well the user-defined field-of-view. The implementation is robust and trustworthy, as long as the view the Kinect is looking from is such that the device clearly distinguishes both legs of the patient. The assessment of the first version of this X-ray simulator reaches the defined goals and expectations and can therefore be used for the purposes initially suggested.

Fig.2: 3D scene and related DRR (X-ray simulation)

Discussion

Restricted, in the scope of this thesis, to rather frontal views of the hip bone, this X-ray simulator has a great outlook potential. This first prototype can lead to further developments that could include the analysis of additional anatomical structures, based on similar or new pose estimations. The possibility of using more Kinects is also of great interest and could increase the final accuracy and robustness performances of the pose estimations. Moreover, possible improvements could lead to the use of this X-ray simulator as a diagnostic device for bone fractures / lesions detection.

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Acknowledgements

Dr. Prof. Philippe C. Cattin's thesis proposal was a challenging and very interesting topic. His continuous support and guidance throughout this project are gratefully acknowledged.

A Content-Based Automated Image Indexer

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Background

The amount of digital images worldwide grows daily. Especially in the medical field, devices such as MRI- and CT-scanners produce a vast amount of data. This makes manual book keeping of image content a cumbersome task. Automated image indexers play an increasingly important role as they allow for indexing and retrieval of specific images *e.g.* for pathology evaluation or statistical purposes. While early indexers relied entirely on additional text-input describing the content, more recent indexers are content-based, where computer vision techniques are applied to analyse the actual content of an image. In this thesis an automated content-based image indexer is presented.

Project Scope

In an initial step, the annotated model stacks are segmented. The SURF algorithm is used to detect keypoints and best matches are found amongst all images. Outliers are removed by Hough voting and a model representation for each slice is constructed. This method also allows for a location voting approach that can predict the location of given points-of-interest (anatomical structures) in an image.

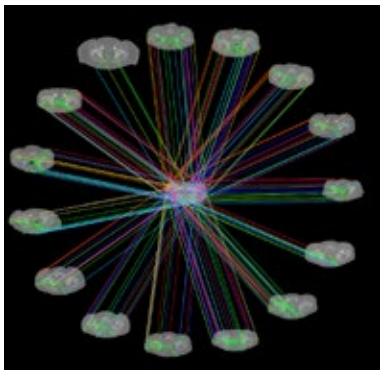
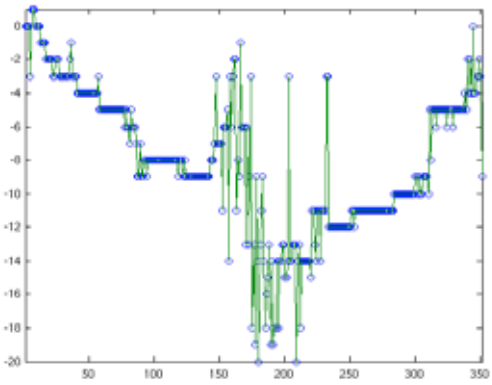


Illustration of the matching step: Each coloured line going from a test image to the reference image in the center represents a matching feature.

Finally, the indexer is integrated into a reliable and fast indexing-framework (Recoll) that allows for straightforward image retrieval.

Results

Experimental data was collected in leave-one-out cross-validation tests. The dataset consisted of 21 full body CT stacks. These were divided into 16 stacks for model creation and the remainder for experiments. Results show a good slice matching accuracy with minor deviations up to 25.5 mm. Location voting shows varying results with average errors ranging from 2.73 pixels to 26.55 pixels depending on the anatomical region.



Results listing the deviations from the predicted to the actual slice location in number of slices.

Discussion

Indexing and retrieval of the CT image works as intended. The Hough voting approach gets rid nicely of outliers to allow for an accurate model representation of each slice. Location voting was extended to support voting for multiple locations in one slice. Investigation into voting-adjustment is needed to support objects with large deformations.

Augmented Reality for CMF Surgery

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Introduction

Invisible critical structures pose a significant risk during complex surgeries. Furthermore, it is important to minimize damage to surrounding structures while as the same time obey the safety margins. The application of augmented reality techniques, displaying the position of the pathologies and critical structures, would be a valuable tool for these surgeries.

Materials and Methods

In this project a cost effective tablet based augmented reality system was developed. Key to the project was its near real-time capability on an off-the-shelf android tablet while being accurate. To find the most suitable algorithms multiple approaches were implemented in Java, C++ and Open GL shading language for comparison to determine the computationally least complex implementation. To simplify the developing and debugging process, a Qt application sharing the same code basis as the Android implementation was developed in parallel.

Figure. 1 Augmented reality - the skull is a real world object; the tumor and the glasses are virtual objects; occlusion object (skull) is enabled thus portions of the tumor within the bone are not visible

Results

The execution of time critical processes could be dramatically optimized by using the appropriate technology. The most time consuming part, the localization of the artificial green landmarks in the camera images, executes now in real-time with a mixture of C++ and Open GL shader code.

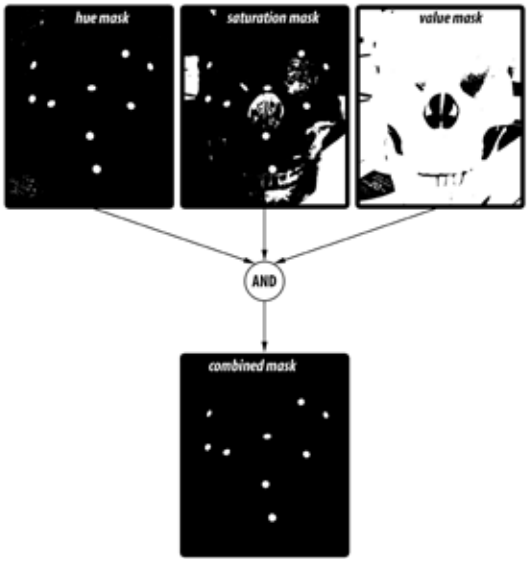

Figure. 2 Logical conjunction of hue, saturation and value mask into final mask used for blob detection

Discussion

The work we have done (see Figure 1) shows that a real-time augmented reality application on today's tablet hardware is possible. Such cost effective solutions increase the usability and mobility of augmented reality systems in medicine.

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In Vivo Biostability / Compatibility of Dynesys® Spinal Implants. A Case Series of 5 Retrieved Implants and Periprosthetic Tissue.

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Background

The Dynesys® stabilization system (Zimmer® Spine, USA) is a pedicle screw based semi-rigid stabilization device, developed as a new concept in the surgical treatment of lower back and leg pain. By stabilizing the spine, but preserving the segmental motion at the same time, negative effects on the adjacent segment should be avoided. From clinical and biomechanical aspects the system has been analyzed in several studies and the clinical midterm outcomes showed good results. Only a few investigations on the in vivo biodegradation and damage mechanisms were performed. Our aim was to determine the in vivo compatibility of the Dynesys® system. To evaluate the tissue response, histo-morphological analyses of periprosthetic tissues were included.

Materials/Methods

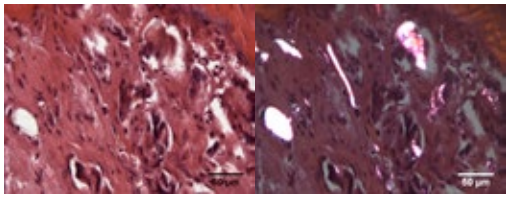
Five retrieved Dynesys® implants with a mean implantation time of 2.86 years (1.9-5.3y) and corresponding periprosthetic tissues gained during revision surgery of the device were analyzed. Histological and particle assessment on the periprosthetic tissue was performed with brightfield microscopy and under polarized light. The implants were optically inspected for surface damage evaluation and chemical changes on the spacer surfaces were measured with fourier transform infrared spectroscopy (FTIR).

Results

All cases showed similar findings with the exception of one case with an implant failure. The histological analysis of the other four cases showed comparable tissue morphologies consisting of regular scar tissue with no inflammation or noteworthy wear debris. Transitional changes from fibrous tissue into fibrocartilage were seen in all cases.

Exemplary findings in terms of surface damages of the implant components.

The implant inspection showed surface damages like scratches and imprints on the polycarbonate urethane (PCU) spacers and some fraying of the outer fibers of the polyethylene-terephthalate (PET) cords. Localized small wear zones on the spacers are attributed to contact with bony structures. The pedicle screws were unremarkable. Changes in the FTIR spectrum of the PCU spacer which might be associated with an altered surface chemistry were only observed in the case of the disrupted cord. The implant failure mode of the disrupted cord could not be verified. In this case the implant failure was clearly associated with massive wear particles accompanied with an inflammatory response of the periprosthetic tissue.



Histomorphological findings of the case with the disrupted cord: Inflammatory response with massive wear debris visible under polarized light.

Discussion/ Conclusion

Excluding the failed implant, our results are comparable with findings of other retrieval analyses. Despite the small case number and the relative short implantation time of this series we would still assume that the performance of the Dynesys® stabilization system is stable and the in vivo compatibility is warranted if the implant does not undergo a major failure.

Effect of Supramalleolar Deformities on the Tibiotalar Joint: Statistical Analysis of the Experimental Contact Forces and Finite Element Simulation

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Examiners: Prof. Dr. Andreas Stahel and PD. Dr. Philippe Büchler

Introduction

Malalignment of the hindfoot has been found to be one of the main risk factors for osteoarthritis (OA) of the ankle joint. It has been suggested that asymmetric OA with frontal plane deformity can be addressed with distal realignment surgery. However, no biomechanical data on the effect of calcaneal osteotomy on supramalleolar deformities has been published and clinical data on the outcome of this procedure is sparse. Therefore recommendations for the treatment of asymmetric osteoarthritis remain arbitrary.

Materials and Methods

The experimental set-up in Figure 1 was configured to assess intra-articular pressure distribution in the ankle joint for various supramalleolar varus and valgus deformities, as well as for distal realignment surgery as an alternative treatment. 14 lower legs (mean specimen age 67) were placed in a loading apparatus with intra-articular pressure sensors in the ankle joint, the deformities and the distal realignment were created and a force of 700 N was applied for 2 seconds recording the static pressure distribution in this time, and the differences among neutral position, deformities, and realignment were analyzed carefully.

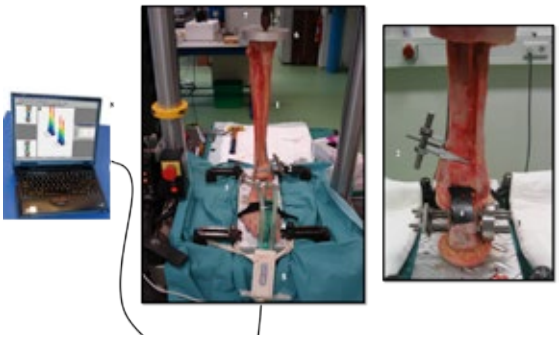

Fig. 1: Experimental Set-up of the study. 1) cadaveric leg, stripped of soft tissue, 2) Wedges of different sizes were used to simulate various degrees of angular deformity in the supramalleolar area, 3) Calcaneal displacement plate to simulated distal realignment, 4) Tekscan 5033 pressure sensor for data recording, 5) Evolution USB Handle 6) Custom plate with a stem attached which inserted into the tibial marrow cavity for axial loading, 7) Instron actuator as the loading apparatus, and 8) K-Scan Software for data visualization.

For the analysis several parameters were computed from the static pressure distribution, such as: centroid of forces, centroid 80% maximal pressure, axial force, and ratio. Three hypotheses were formulated:

1) Inframalleolar and supramalleolar deformities affect the ankle joint load distribution differently.

2) Calcaneal osteotomies affect the load distribution in both, mediolateral and anteroposterior, direction.

3) Calcaneal osteotomies in supramalleolar deformities do not normalize the ankle joint load distribution.

The Finite Element Method (FEM) could provide an ideal vehicle for the study of joint contact stresses on a patient-specific basis. Therefore, successful cadaver validation would provide a strong support for FEM model biofidelity. The purpose of the simulation was to assess whether static pressure distribution of the neutral position measured experimentally could be reproduced using a FEM numerical model based on generic.

Results and Discussion

The purpose of this biomechanical study was to determine the effect of simulated supramalleolar varus and valgus deformities, and distal realignment surgery by a calcaneal osteotomy on the ankle joint load distribution.

Hypothesis 1): Although the overall alignment of the lower extremity is the same, e. g. same offset of the calcaneus with respect to weight bearing axis, the changes in the ankle joint are different in supramalleolar and inframalleolar deformities.

Hypothesis 2): We found that non-anatomical alignment correction of the hindfoot does not restore the ankle mechanics in the *invivo* model. Therefore isolated calcaneal osteotomies, which have been successfully used to treat hindfoot deformities such as cavovarus or planovalgus feet, may not be appropriate for the treatment of ankle arthritis.

Hypothesis 3): A significant finding is paradoxical pressure distribution after calcaneal osteotomy, inframalleolar valgus deformity lead to anteriomedial pressure overload. In inframalleolar varus deformity postero-lateral pressure overload is observed. Previous works were reviewed and two main differences between the experimental set-ups were established: on one hand, amputated lower legs were used and on the other hand, the subtalar joint was connected with the talus by means of K-wires.

A simple comparison of the FEM model with the experimental data establishes accordance in the contact stress distribution, but a large difference in the maximal pressure value. The non-natural stress concentration may be caused by irregularities of the mesh where a sharp-pointed node could prevent the solver from performing an accurate contact analysis.

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Acknowledgements

I wish to thank my supervisors, L. Bolliger and W. Businger for their encouragement and guidance throughout this project.

Bern University of Applied Sciences
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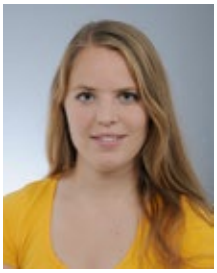
Engineering of Structured Scaffolds for Cartilage Regeneration

Nina Ruef



Supervisors: Dr. Jorge Sague and Dr. Reto Luginbuehl
Institutes: RMS Foundation, Bettlach
Examiners: Dr. Reto Luginbuehl and Prof. Dr. Benjamin Gantenbein

Introduction

Osteoarthritis is a degenerative, inflammatory joint disease that is very common in elderly people. There are several joint-preserving treatment methods available, but outcome of therapies vary largely and long-term results are unsatisfactory in the majority of cases. Cartilage tissue engineering based therapies might be an alternative to conventional treatments and they have shown some promising results for cartilage regeneration, but in most cases the *de novo* and repaired cartilage is not satisfactory regarding its structure and its mechanical properties. Scaffolds which are currently explored for cartilage engineering do mostly not have a specific orientation and do not support and stimulate the formation of a mechanical competent tissue.

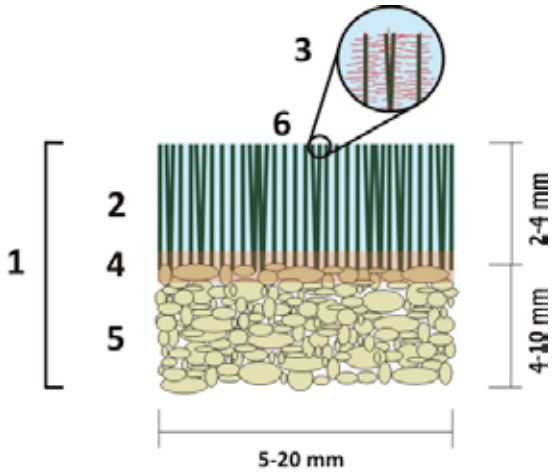


Fig. 1 Schematic of the scaffold with highly oriented fiber component (2), fiber functionalization (3), binding interface (4), mineral anchor (5), and hydrogel backfilling (6)

It was the aim of this thesis to develop a prototype of a highly oriented scaffold for cartilage regeneration comprising multiple components (**1**). This scaffold should mimic the structure of healthy articular cartilage tissue and thereby support the regeneration of mechanically competent cartilage.

Materials and Methods

Different natural and synthetic polymeric fiber materials, including polylactic acid and cellulose, were evaluated for the use in the fibrous component of the scaffold (**2**). Methods were explored to functionalize the surface of fibers which enable subsequent grafting of biocompatible molecules (**3**). Polymer surfaces were altered by chemical oxidation, hydrolysis and by a photochemical approach and analyzed in infrared spectroscopy and X-ray photoelectron spectroscopy. Different possibilities to align fibers and to attach them perpendicular to the surface onto a ceramic anchor (**5**) were elucidated, and the resulting interfaces (**4**) were investigated. An injectable two-component hydrogel was developed as backfill for the fibrous part (**6**). It is based on a combination of chitosan and dextran which doesn't require an additional crosslinking agent Mechanical compression tests were performed to compare scaffolds without hydrogel backfilling to ones scaffolds with hydrogel backfilling.

Results and Discussion

It was demonstrated that it is feasible to engineer scaffolds with the proposed highly structured organization mimicking native articular cartilage. The fibrous part, with polymer fibers aligned perpendicularly to the surface, was successfully attached onto a porous ceramic anchor. It was possible to assemble such a scaffold from completely biodegradable materials, when using PLA fibers and a β-TCP anchor, connected by localized melting of the PLA fibers. Chemical derivatization allowed for introducing functional groups for subsequent immobilization of biomacromolecules. The hydrogel backfilling system increased the stiffness of the assembled device significantly by 155% for PLA and 48% for cellulose based scaffolds, respectively.

Outlook

Future cell studies will have to be carried out testing biological performance of the assembled scaffold, i.e. with regard to cell seeding, cell viability, phenotype stability, extracellular matrix deposition, and integration within the surrounding tissue.

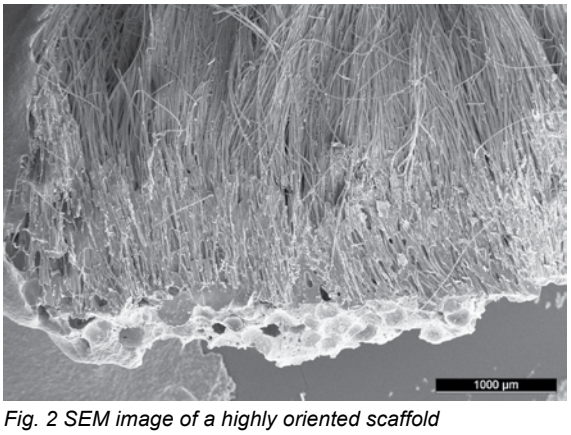


Fig. 2 SEM image of a highly oriented scaffold

System for Real-Time Depth Measurements During Orthopedic Operations

Anton Niklaus Schärer

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Examiners: Prof. Dr. Volker M. Koch and Prof. Dr. Jörn Justiz

Introduction

Depth measurement is indispensable during orthopedic surgeries. After drilling a hole through or in a bone, the surgeon needs to know the depth of it in order to choose the correct screw length. Depending on the anatomic spot, this decision is crucial and can lead to bad fixation or even to severe damage of nerves, joints or blood vessels. State of the art measurement is done after drilling (mechanically) and requires experience. X-ray is needed 20 - 40 times per operation to check the actual drill position or the final screw placement. Often screws must be replaced afterwards. In order to minimize operation time and x-ray exposure a system for real-time depth measurement is developed.

Materials and Methods

1) State of the Art Analysis & Principle Evaluation

The evaluation of the study of principles takes into accounts not only the engineers', but also surgeons' as well as industries' views. These are obtained by interviews with people working in the field and a survey among orthopedists. The resulting most promising principle is based on the electromagnetic induction of co-axial solenoids, which is influenced by a metal ring, fixed on the drill.

2) Prototype Design

Material research is required to find beneficial steels for drill and core. By using simulations based on FEM the beneficial parameters for the prototype are found. The prototype is then realized using rapid prototyping and self-made coils.

3) Prototype Validation

A measurement environment has been set up, which allows calibrating of the sensor as well as control-measurements.

Results

Figure 1 depicts deviations from five different measurements in relation to the actual drill depth. All measurements are in the range of ±0.4 mm and are even much more accurate between 15 mm and 45 mm where deviations are less than ±0.2 mm.

The calibration is expected to be long-term stable at least within the scope of days. The observed trends are explained with the change in length of the primary coil due to changes of temperature caused by the current, but they are not related to the time of calibration.

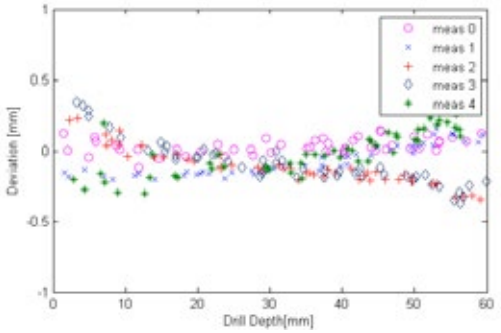


Fig. 1: Deviation for five measurements within six days.

In the final prototype, an excitation coil frames two receiver coils that are wound in opposite sense to increase the sensitivity in detecting the perturbation due to the metallic core (see Figure 2).

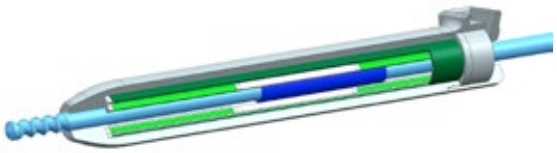


Fig. 2: CAD sketch of the prototype.

Discussion

The overall objective, namely to design a working prototype which is capable to measure in real-time the depth of a drill hole, has been reached. Furthermore the device meets the demands, hence is reliable, easy to use and accurate enough. However, a further improved prototype should use a scaffold out of a rigid, temperature stable material such as PEEK. Furthermore it should comprise a metallic covering which prevents the device from environmental influence. The accuracy of such an improved device is estimated to be ±0.15 mm.

Further work must inevitably include investigations concerning the sterilization capabilities. These are dealt with only theoretically in the present study. It is reasonable to do further investigation with an industry partner. The aim is to extend the device's function insofar that it could additionally sense the drills environment and thereby detect or prevent a break-through.

Preformed Cranial Implants

Saloni Soin

Supervisors: Kurtis Wheeler
Institutions: Synthes GmbH CMF
Examiners: Prof. Dr. Stephen Ferguson and Dr. Mauricio Reyes

Background

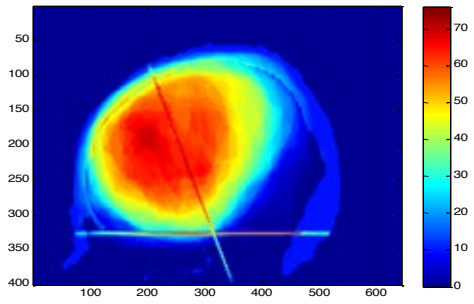
Cranial bone defects occur as a result of trauma, tumor resection surgery, and infections involving the cranial bone necessitating its removal. After the removal or trauma of the bone, the patient is left with a non- symmetric skull and undesired symptoms. Being of clinical as well as cosmetic importance, cranioplasty is performed to reconstruct the bone restoring the protection of the brain and improving the appearance of skull surface.

As an option Preformed Cranial implants can be used for cranioplasties. These devices are modified by the surgeons according to the defect. These implants are less expensive and off the shelf available eliminating the waiting time.

Project Scope

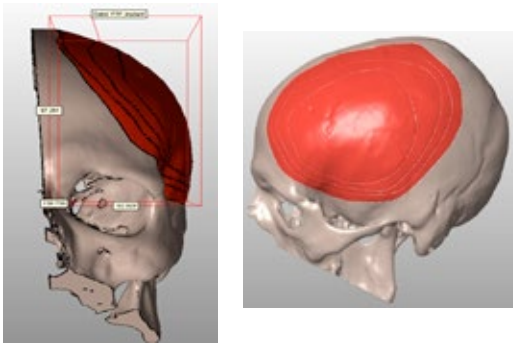
The aim of this project was to determine shape, size and location for the most common cranial defects in order to be able to design preformed cranial implants, which fit the majority of cranial defects across the majority of the adult human population.

Method and Results



80 Frontal- Temporal Parietal defects overlapped after registering them onto same coordinate system.

The method proposed in this study gives information about the anatomical regions of the cranium and the frequency of defect occurrence in those regions. It offers a way to measure the defects by means of projections allowing obtaining their average sizes and locations. Employing non-rigid registration, overlapping and image processing techniques yield the average shape of the defects. Statistical analyses were used to give value to the acquired results. At last the average sized and shaped defects were transformed back to three dimensions to be able to design for the final implants.



Frontal-Temporal-Parietal shape and region in 3D, indicating different statistical coverage.

Discussion

To date no other study has reviewed this kind of information using defected skulls. Therefore, the proposed methodology is unique and provides information about the size, shape, and location of the defects.The simplicity of the method ensures the transferability as it can also be used for any other indication or anatomy with missing bone. The obtained results can easily be expanded to allow for multiple sizes of implants in different anatomical regions.

Design of One-Dimensional and Two-Dimensional Functional Cell Culture Models with Polarized Mammary Epithelial Cells

Thomas Stuebi

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Institutions: University of Bern, Institute of Biochemistry & Molecular Medicine
Examiners: Prof. Dr. Christiane Albrecht and Prof. Dr. Wilhelm Hofstetter

Background

After birth, mammals nourish their offspring with milk. The milk composition varies among species, and fat is the third important constituent. Cholesterol as part of this milk fat fraction is important for the milk secretion process in the mammary gland.

Constituent per L	Early milk	Mature milk
Lactose (g)	20-30	67
Oligosaccharides (g)	22-24	12-14
Total protein (g)	16	9
Total lipids (%)	2	3.5-5
Triglycerides (% total lipids)	97-97	97-98
Cholesterol (% total lipids)	0.7-1.3	0.4-0.5
Phospholipides (% total lipids)	1.1	0.6-0.8
Fatty acids (weight %)	88	88

Human milk constituents, adapted from Kleinmann, 2009.

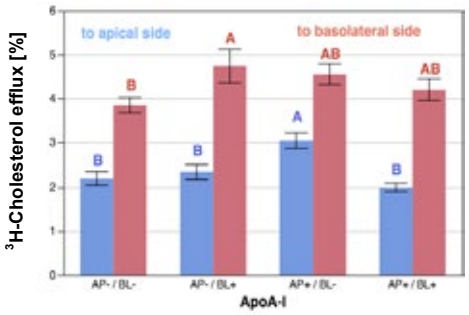
In different studies regarding the mechanism of cholesterol transfer into milk, energy dependent processes involving ATP-binding cassette (ABC) transporters are described. Based on the subcellular localization in bovine mammary tissues, ABCA1 is supposed to play an important role in this physiological process. In macrophages ABCA1 is known to transfer cholesterol to specific acceptors such as apolipoprotein (apo) A-I.
To further investigate this topic in mammary epithelial cells, functional cell culture models are needed.

Project Scope

The present work focused on the establishment of appropriate methods to allow an analysis of active cholesterol transport in mammary epithelial cells. Starting with the evaluation of cell culturing parameters, the setup of a 1-dimensional as well as a 2-dimensional cholesterol efflux model was planned. Prior to bidirectional cholesterol efflux experiments, methods to assess the tightness of cell monolayers grown on the Transwell® system were necessary.

Results

With the optimization of the cell culturing methods, the facility to investigate active cellular cholesterol efflux was accomplished. Tight epithelial monolayers were achieved and according measurement techniques to assess the permeability were successfully introduced. Confounding factors in liquid scintillation counting were found and eliminated. The apoA-I mediated ^{3}H-cholesterol efflux in the 1-dimensional model with different cell types and in the 2-dimensional model with MeBo cells was repeatedly measured.



Result of polarized cholesterol efflux with MEC. Levels not connected by the same letter are significantly different (not across apical and basolateral values).

The dependency of the ^{3}H-cholesterol efflux on the gene expression of ABCA1 in mammary epithelial cells was not revealed so far. Therefore several aspects with respect to cellular processes and signaling pathways were evaluated using the developed model.

Discussion

Even though a conclusive appraisal of the ABCA1 dependent and apoA-I mediated cholesterol efflux is not yet possible, the results obtained in this work allow the development of consecutive strategies to get more insight into active cholesterol transport mechanisms in mammary epithelial cells.

Parylene Multilayers for Miniaturized Implantable Devices

Stefanie Uhl

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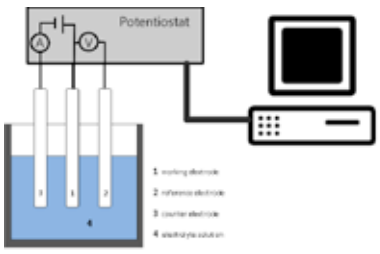
Institutions: Codman Neuro Sciences Sàrl
Examiners: PD Dr. Jürgen Burger and Prof. Dr. Herbert Keppner

Background

State of the art packaging for implantable devices use metal and glass housings that are reliable but limited in miniaturization and cost-intensive. In the framework of a CTI project, a new packaging based on Parylene Multilayers is under development. In order to characterize the hermeticity of the manufactured Multilayer packaging a helium diffusion setup was developed to measure the permeation of Helium through the Multilayers. Implants face an environment which includes blood and other constituents of the body fluid, therefore the performance of the coating needs to be also characterized in a close-to-realty environment.

Project Scope

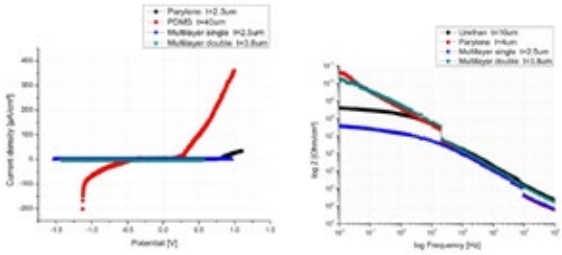
The electrochemical methods 'Polarization Measurement' and 'Impedance Spectroscopy' were applied in order to study the ion-transport through and the degradation of the coating on a stainless steel sample. The measurement setup and protocol were developed on the base of the medical standards ASTM F746 and F2129 as well as publications for the evaluation of bio-corrosion. A defined area of the test sample was exposed to a physiological solution, which represents the working electrode of the electrochemical cell setup. The characterization parameters are the development of the open circuit potential over time, the current density during polarization and the impedance of the coating at different frequencies.



Electrochemical cell with a three electrode setup

Results

After a short-time immersion the Multilayer coatings did not show any corrosion current when polarizing the test sample. However, the long-term immersion revealed corrosion current and a layer delamination from the substrate. Moreover, it was seen that the samples are not reproducible. With an improved adhesion a reproducibility of the open circuit potential could be shown.



Potential-Current Density Curve (left); Bode Plot of Impedance Spectrum (right)

The Impedance Spectra of the Multilayer coatings as well as the Parlyene reference samples revealed different degradation states. After short time immersion both coatings reached standard impedance values, however with long-term immersion delamination appeared.

Furthermore, the performance limits of the potentiostat have been reached, which was shown through the disturbances in the measurement signal.

Discussion

It has been found that the behavior in liquid is much more complex, than the previous characterization with helium gas. The investigation showed that deposition parameter must be optimized for a better adhesion of the coating on the substrate and between the different layers. The Multilayer impermeability, however, is already in a range where more current sensitive measurement equipment is necessary for the characterization.

Development of Bending Device for the Visualization of Microcracks in Cortical Bone

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Institutions: Institute for Surgical Technology & Biomechanics, Universität Bern
Examiners: Prof. Dr. Philippe K. Zysset and Dr. Uwe Wolfram

Introduction

Osteoporosis is a major health problem. 30% of all women and 20% of men are affected by the disease. Osteoporosis is characterized by a loss of bone mass and results in a decrease of mechanical competence and a higher risk fracture. Finite element simulations would be very helpful for the prediction of fracture risk, their capability to model the damage behavior needs to be validated. Damage in bone occurs in the form of microcracks increase the risk of fractures. Currently no method is available to quantify their evolution properly in bone. For this purpose an experiment was developed to load bone specimens in a custom made four point bending rig with simultaneous staining with fluorescent dyes of the induced microcracks.

Materials and Methods

Bovine bone specimens were first monotonically loaded to failure. Then, cyclic tests with different dyes in two loading directions were performed to visualize the propagation of the microcracks. Multiple cross and longitudinal sections of stained bone specimens were then prepared with an ultra miller and images were taken with an epifluorescent microscope to show the propagation of the microcracks.

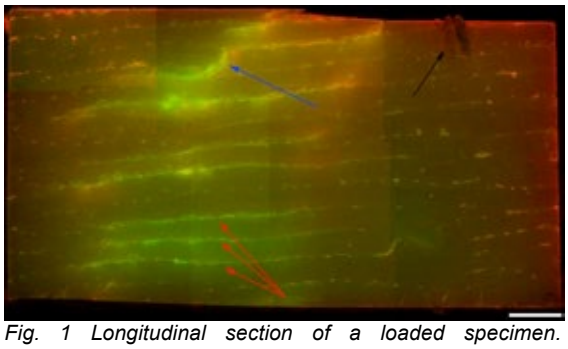

Fig. 1 Longitudinal section of a loaded specimen. Longitudinal (red arrows) and cross-lamellar cracks are observable (blue arrows). The red dye was applied during the first loading, the green dye during the second loading cycle. Scale bar = 500 µm

Results

Microcracks can be observed in the tested specimes. The two applied fluorescent dyes (Xylenol Orange and Calcein Green) stained the propagating microcracks. The serial sectioning technique allowed us to visualize the propagation of microckracks in multiple cross and longitudinal slices.

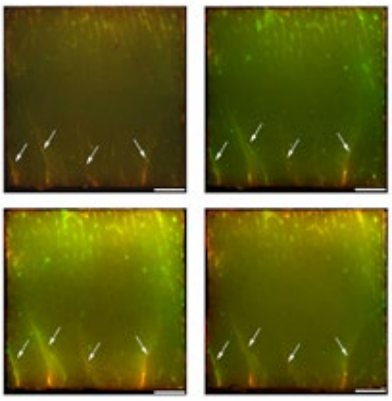

Fig. 2 Cross-section series of a tested and stained specimen. Propagating microcracks (white arrows) are observable and stained with two different dyes (red and green). Scale bar = 500 µm

Discussion

The staining with two dyes worked as expected. Nevertheless it is a problem that dyes tend to bleach out leading to a reduced fluorescence. The developed process is very time consuming and an automatic system would be useful.

References

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Acknowledgements

The support of Dr. Fabian Blank and Dr. Jens Stein for the micoscopy and the important contribution of Urs Rohrer and Alexander Bürki for construction of the experimental set-up is gratefully acknowledged.

Evaluation of a Motion Tracking System for Gait Rehabilitation Robotics

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Examiners: Prof. Dr. Tobias Nef and Markus Spindler

Introduction

Real time 3D motion tracking is a common problem in many fields of industry and science. Most of the methods known are expensive and not universally applicable to different environments. The basic motivation for this study is to solve the pose estimation problem for the end-user in a simple way. Furthermore, the solution should be at low cost and universally applicable.

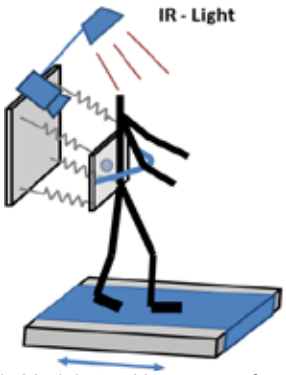

Fig. 1 Pelvis Module tracking system for gait rehabilitation

The backgrounds for this study are the new developments for the gait rehabilitation robot Lokomat. It is developed by the company *Hocoma* for patients with stroke or spinal cord injuries. This robot is mainly used to care for patients after their injuries. New concepts were developed that allow more degrees of freedom than the conventional systems, to improve the balance training for the patients. One of these concepts is the Pelvis Module, which is a guidance of the pelvis. The additional degrees of freedoms force the patient to balance but still support him. The movement of the pelvis plate is not known since it is attached to the pelvis and depends on each patient. Therefore a pose tracking system was evaluated.

Materials and Methods

To address the problem of the pelvis plate, requirements were defined for a tracking system in a gait rehabilitation robot environment and different tracking principles were evaluated. The evaluations lead to realization of a monocular optical pose tracking system with a planar marker.
The system consists out of a computation unit with software, an industrial camera with infrared light source and a marker, compare Fig 2.

Fig. 2 Hardware of planar marker tracking system

For the gray scale camera a marker detection and a pose reconstruction software was developed and state of art algorithms were implemented. The code was written in C++ and the image processing library, Open CV, with real time capabilities was used.

Results

Different measurements were undertaken to determine the accuracy of the system. For example a 100 mm side length marker was moved on different locations of the x-z camera plane. Fig. 3 shows the results for this measurement.

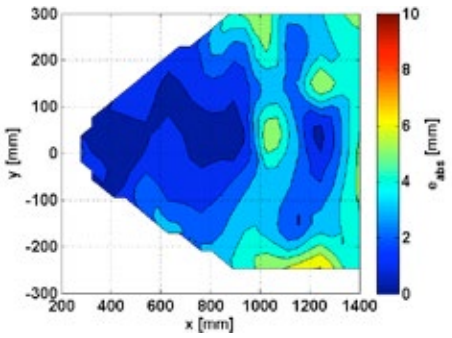

Fig. 3 Position error of a marker with 100mm side length

Discussion

The resultant system showed that it is applicable for pose tracking in the Pelvis Module application. A sub-millimeter accuracy in the close field was reached. The system gives also information about the orientation of the marker. However, the direction dependency of the system has to be taken into account in system design and especially in the farer field where the system suffered from various factors that influence the accuracy.

Morphological Determinants of Hip Instability

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Institutions: Institute for Biomechanics, ETH Zürich
Examiners: Prof. Dr. Stephen J. Ferguson and Prof. Dr.-Ing. Lutz-P. Nolte

Introduction

The ideal human hip joint is free of any instability. A stable hip joint has a highly congruent articulation between the femoral head and the acetabulum. The stability of a hip joint may be lost when the shapes and orientations of acetabulum and femur deviate from the normal anatomical values. Instability may provoke a dislocation of the femoral head, causing a focal overloading of the articular cartilage. In extreme cases, a total subluxation of the hip joint is possible. In repeated instances of cartilage overload, osteoarthritis in the hip joint may arise, causing pain and immobility of the patients (Ganz 2008).

To date, knowledge on the biomechanical link between hip joint morphology and joint stability is limited. Therefore, the goal of this study was to observe the influence of the *acetabular index*, the *acetabular version* and the *femoral anteversion* on the joint stability and the internal mechanical response of the joint.

Materials and Methods

To investigate the influence of these parameters, geometrical models with variations in the morphological parameters were created to perform finite element (FE) simulations. The load and motion patterns used for the simulations were derived from *in vivo* data measured in real time, obtained from the Orthoload project (Bergmann 2012). The performed simulations included a step during a normal gait cycle and a standing-up motion.

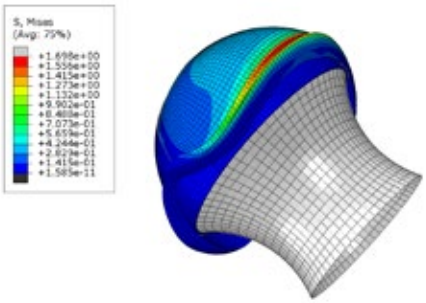

Fig. 1 Abaqus FE simulation model displaying the healthy hip joint with the von Mises stresses at the time of the maximum loading during a gait cycle.

During the simulations, the von Mises stress in the acetabular fossa and rim, the contact pressure on the inner face of the acetabulum and the dislocation of the femoral head were determined.

Results

The results showed a clear influence of the acetabular index and the acetabular version on joint stability. Increased values in both parameters dramatically decreased joint stability. An influence of these parameters on the stresses and contact pressure was clearly observed, especially in the gait cycle simulations. An influence on the impingement risk was mainly observed in the standing-up simulations.

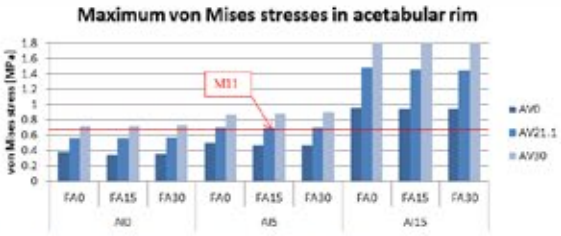

Fig. 2 Maximum von Mises stresses of the different models during a gait cycle in the acetabular rim. AI: Acetabular index, AV: Acetabular version, FA: Femoral anteversion, followed by its degrees. M11 labels the healthy hip joint.

Discussion

The results of the study showed the combinatory effect of the anatomical parameters considered in the study and its effect on mechanical responses in the hip joint. It was shown, that an increase in the acetabular index and version lead to an unstable hip joint during a normal gait cycle. The results also showed that such unstable hips were less prone to dislocations in the standing-up motion cycle, due to the high muscle forces which stabilize the hip joint. On the other hand, a reduction of the acetabular index and version increased the risk of an impingement in the standing-up simulations. The influence of femoral anteversion showed the same trends, but with smaller effect.

The stress and contact pressure behaviors were highly dependent on geometry and orientation of the acetabulum and the load pattern. Large differences were observed between gait cycle and standing-up simulations. Changes in the parameters usually shifted the stresses in the acetabular fossa to the rim or vice versa. The hips having normal geometry and orientation of the acetabulum have optimized anatomical parameters to perform common daily activities without risks of joint overload or dislocation.

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Bergmann, G., HIP98, 2012

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Energy Management System for a Leadless and Batteryless Cardiac Pacemaker

Jörg Wagner

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Institution: ARTORG Center for Biomedical Engineering Research, Universität Bern
Examiners: Prof. Dr. med. et. phil. nat. Rolf Vogel and Prof Dr. Marcel Jacomet

Introduction

Electrical medical implants such as defibrillators, neurostimulators and pacemakers use primary batteries as their energy source. The amount of energy storable by these batteries is a limiting factor of implanted devices. Hence, some patients need several device replacements during their lifetime. These replacements are expensive and bear the risk of infections.

The aim of this study was to examine the feasibility of powering a pacemaker by an existing energy harvesting device which is based on the clockwork of a commercially available automatic wristwatch. The energy harvester's main component is an oscillating mass that gains energy from the cardiac movement. A micro-generator converts the mechanical energy into electrical energy in the form of short electrical impulses (Fig. 1). To be able to power a pacemaker from these impulses, an energy management system is required to extract, condition and store the energy.

Materials and Methods

A mathematical model was developed to simulate the behaviour of the energy harvesters output impulse. This allowed the assessment of different energy extraction methods for the energy management system. Based on these simulations, a concept for an energetically efficient management system was developed and realized in a prototype (Fig. 2). The design of the prototype is based on discrete electronic parts which were evaluated in terms of their internal power consumption.

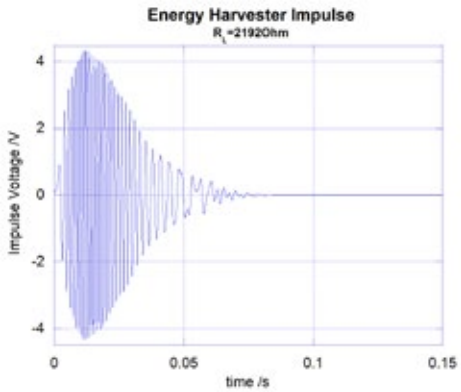

Fig. 1: Impulse of the energy harvester over a load resistor of 2182 Ohm.

In a former animal study, the energy harvester delivered twenty impulses per minute. With the impulse energy content of 80 µJ this leads to a maximal output power of 26.7 µW. Infered from measurements and literature, the minimal power consumption of commercial pacemakers was estimated to be around 20.6 µW for asynchronous pacing. However, commercial pacemakers provide lots of power consuming features that are not directly related to the pacing. The required pacemaker output power for asynchronous pacing is about 9.4 µW.

Results

For the validation of the concept, an asynchronous pacemaker was integrated into the prototype. This custom-made pacemaker provides a lower housekeeping power consumption than commercial pacemakers. It was possible to extract and store 73.8% of the energy provided by the energy harvester. This corresponds to a power of 19.7 µW. Depending on the pacemaker's load, a pacing output power up to 17 µW can be achieved.

Discussion and Conclusion

Measurements with the prototype were consistent with the simulations and showed that the energy management system is capable of extracting and buffering enough energy from the harvester to supply this pacemaker. An in-vivo study is intended to confirm the final proof of concept.

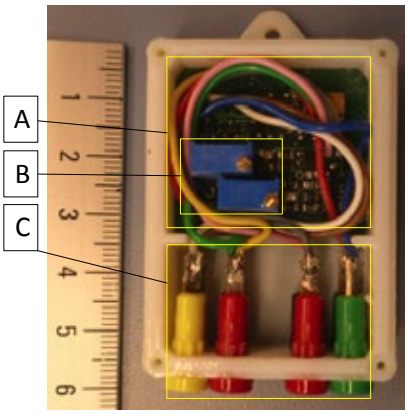

Fig. 2: Top view of the prototype with removed cover plate. (A) PCB with the energy management and the pacemaker. (B) Trimmers for adjustment of the pacing rate and pulse width. (C).Connectors.

Automated Tests for Electrical Impedance Tomography

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Introduction

Electrical impedance tomography (EIT) is a non-invasive imaging technique that displays the spatial distribution of the conductivity of a body from surface electrical measurements.
Several different EIT devices are available from academic and commercial suppliers. Although some groups have proposed performance analysis methods as well as phantoms, a robust, standardized, and automated test system for EIT systems is still missing. This prevents fair comparisons between systems, easy and extensive testing and rapid product development iteration cycle.

Materials and Methods

The performances of EIT devices are tested on a cylindrical tank filled with a water-based NaCl solution. It is equipped with a total of 32 electrodes. A dedicated circuit, the contact impedance module, can be connected between each tank electrode and the corresponding EIT device electrode. This circuit is able to generate 9 different contact impedance scenarios for each of the 32 electrodes. In order to achieve precise and reproducible measurements while minimizing human error, we use an industrial robotic 6-axis arm to place test objects at different positions inside the tank. The complete test system is driven by PC software, which defines object placement, contact impedance scenarios and EIT data acquisition schemes.
Various image quality indexes – positioning error (PE), area error (AE) and shape deformity (SD) – are used to compare different current injection patterns and image reconstruction parameters.

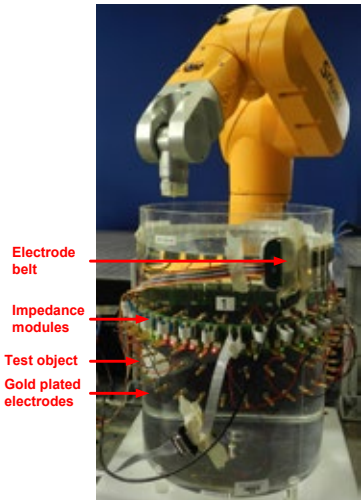

Fig. 1. Overview of the test system including an EIT electrode belt, a robot and a contact impedance module.

Results

Current injection patterns using small-angled injection pairs (i.e., electrodes close to each other) show a poor performance. On the other hand, large current injection angles lead to high errors. Good performance with lowest total errors is found at angle 56°, 79° and 101°. Figure 2 is used as an illustration of one positioning error map.

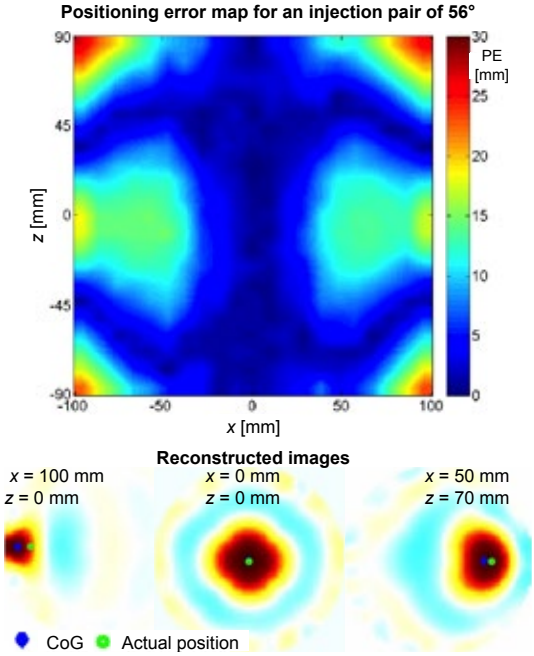

Fig. 2 Upper part: positioning error map for an injection pair of 56°. Lower part: In three reconstructed images for a calibrated non-conductive test object, the actual position, green, and the center of gravity (CoG) – blue – are marked. Red indicates a high impedance area.

Discussion

The main advantage of the developed test system lays in the complete automation. This enables long and fastidious experimental protocols to be followed and repeated each time modifications are made to an EIT system. Thus the quality of the delivered images can be accurately analyzed. Moreover, it can also be used to optimize the measurement and image reconstruction strategy based on the measurement of the image quality indexes PE, AE and SD.

Acknowledgements

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Gaze Tracking System for Ophthalmic Devices

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Introduction

Examinations of eyes, such as topography measurements or visual field tests, can be delicate due to the fact, that the reliability and accuracy of the results strongly depend on the gaze direction of the appropriate eye. The longer the measurement takes, the harder for the participant to keep the gaze at a certain point of fixation. To prevent and avoid measurement errors, some devices feature a semi-automatic supervision possibility by providing a top-view camera. Gaze trackers come into play when a fully automatic supervision of the subject's line of sight is desired. We propose an optical gaze tracking system on the basis of a compact frame construction, typical for an ophthalmic device.

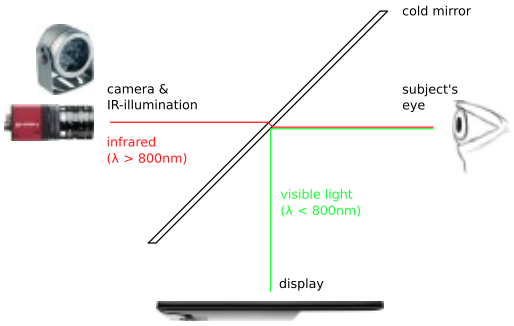

Fig. 1: Basic setup principle.

Methods

In order to fulfil the needs of ophthalmic applications, while keeping flexible and having extension possibilities, we introduce an eye model, based on the method of E.Guestrin and M.Eizenman. The 3D model of the eye includes also its environment, consisting of a display, a camera and an infrared illumination. The process of obtaining a gaze estimate based on a camera image showing the eye of a subject can roughly be divided into 3 steps:

- Image acquisition & preprocessing
- Feature detection: find pupil & glint centres
- Model evaluation & gaze estimation

The first two points particularly deal with image analysis and processing, whereas the third point of the list is about evaluating a ray tracing based eye model. This model evaluation includes the sequential reconstruction of the optical and the visual axis of the eye. After that, it's possible to calculate the point of gaze, which is located on the visual axis where the eye has its focus on. Moreover, the model eye has to be fitted to the subject by adapting some anatomical parameters through a calibration procedure.

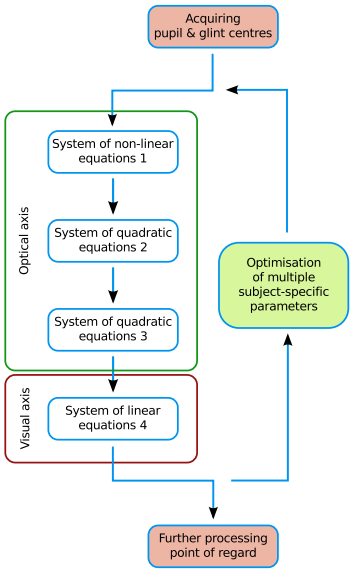

Fig. 2: Overview of gaze estimation algorithm.

Results & Discussion

Our experiments have shown, that we are able to estimate the point of gaze of a certain subject with an accuracy lower than 1°. This angle corresponds to an average deviation between the point of gaze estimate and the true point of gaze, measured at the rotation centre of the eye. This value is comparable to accuracies of commercial eye trackers. Our system is, however, sensitive to even small eye position changes. To overcome this limitation, the model could be extended by additional light sources. We believe that this would lead to a higher robustness of the model and even a higher accuracy value.

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